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## THE COMPLETE ELIMINATION OF RETROLENTAL FIBROPLASIA\*

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IN SPITE OF ADVANCES in preventive knowledge, cases of retrolental fibroplasia (RLF) are continuing to occur, and the problem of blindness in infancy from this disease is still a serious one.

During the past year, we have seen or heard of some 15 new cases in the Montreal area, and from conversations with colleagues in other parts of North America it is apparent that the problem of sporadic cases is a general one.

In previously reported experiences,<sup>1, 2</sup> a dramatic decrease in the incidence of RLF was achieved by reducing to minimal safe levels the amounts of oxygen given premature babies. Nevertheless, even after the institution of this policy, six out of 118 babies weighing 4 lb. or less at birth developed the disease, and in two of these the condition was severe (loss of useful sight in both eyes).

In the present paper, we are able to go a step further and report the complete absence of the disease, in all its stages, in a group of 126 babies born between July 1954 and the present, after the addition of certain essential safeguards to our previous low oxygen policy. These experiences now lead us to believe that retrolental fibroplasia is entirely preventable, and that all future cases must be assumed to be due to human or mechanical error.

### MATERIAL AND METHODS

Table I shows the birthweight distribution of the 126 infants included in this study. These

TABLE I.—BIRTHWEIGHT DISTRIBUTION OF 126 PREMATURE INFANTS WHOSE OXYGEN WAS CAREFULLY CONTROLLED AND WHO DEVELOPED NO MANIFESTATIONS OF RETROLENTAL FIBROPLASIA

Birthweight (lb.)	No. of babies
2½ and less	17
2½—3	19
3—3½	38
3½—4	52
Total	126

comprise all surviving babies weighing 4 lb. or less at birth, born at the Women's Pavilion of the Royal Victoria Hospital and at the Catherine Booth Mothers' Hospital between July 1954 and December 1956, who had their oxygen controlled according to the principles described below.\*

### USE OF OXYGEN

No curtailment of oxygen was felt necessary for resuscitation. However, as soon after delivery as possible, the infants were transferred to incubators, usually an Isolette, where oxygen was given only for one or more of the following signs:

1. *Cyanosis of arterial blood desaturation.*—This must be differentiated from the blueness of hands and feet commonly seen in newborns, and from the blueness of head and neck following rapid delivery or constriction of the neck by the umbilical cord.

2. *Respiratory distress.*—This is manifested by rapid respiration associated with "indrawing" of the subcostal region or of the sternum itself. Moaning or grunting often precedes the onset of frank indrawing. Irregular respirations *per se* are, of course, no indication for oxygen therapy.

\*Four babies were excluded. In three, the oxygen concentrations were not measured. In the fourth, an infant with early respiratory distress, high oxygen (40-50%) was ordered by the private physician, and the order was not amended for 36 hours. Oxygen concentrations were recorded irregularly, but reached as high as 60%, in spite of normal colour and normal respirations. This baby and one of the three who received oxygen in uncontrolled concentrations showed early mild changes (Stage I active RLF), which regressed. The fundi of both returned to normal, and normal vision is predicted.

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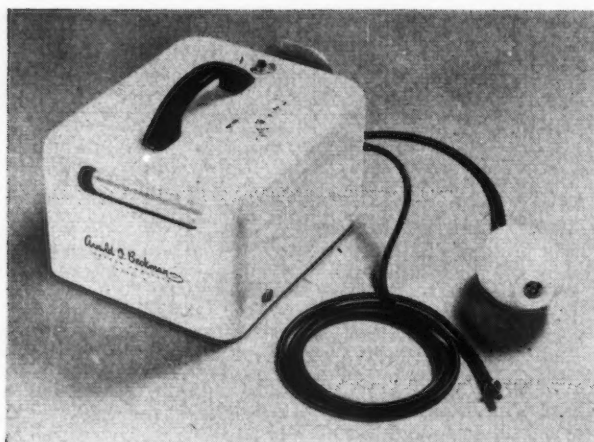


Fig. 1.—Beckman Model D oxygen analyzer.

3. *Poor colour and reduced activity after oxygen cessation.*—This was sometimes the first sign of an infection.

4. *Pallor after feedings.*—In some very small infants a striking pallor is noted shortly after feedings. This was treated with oxygen.

The decision whether or not a baby needed oxygen was made by the nurse in charge, until such time as the paediatric intern, the attending paediatrician, or one of the authors saw the patient.

When oxygen was required, its concentration was not permitted to exceed 40%, unless the baby remained cyanotic or continued to show severe respiratory distress at this level. This occurred rarely, and then usually only for a

short time. In a few such instances, a Sekelj ear oximeter was used. When this showed that the arterial blood was not fully saturated, in spite of the baby's exposure to 40% oxygen, this concentration could be exceeded with greater confidence.

No long-standing orders for oxygen were written. The nursing staff had instructions to reduce it and then discontinue it as soon as possible.

Oxygen concentrations were measured, on the whole, once every two hours, day and night, using a Pauling-type Beckman Model D oxygen analyzer (Fig. 1). They were recorded on a special oxygen sheet with remarks about the infant's colour and respiratory activity (cf. Fig. 2). More frequent measurements, as often as once every 15 minutes, were made after initiating oxygen, changing its rate of flow, or opening the incubator lid or sleeves. At such times, concentrations higher than 40% would occasionally be recorded and the necessary adjustment quickly made. Figs. 3 and 4 show graphically examples of oxygen history.

Although the oxygen flow was generally controlled with a ball flowmeter, the Rotameter flowmeter, which accurately controls flow rates below two litres per minute, was in frequent use.

Compressed air was available for use with the Vapojet attachment, when it was felt that added moisture and not oxygen would be of most benefit to the infant.

#### EYE EXAMINATIONS

Weekly ophthalmoscopic examinations were performed after dilatation of the pupils with one drop each of 2% homatropine hydrobromide and 10% Neosynephrine (phenylephrine) hydrochloride. They were carried out from the time the baby was sufficiently robust until his discharge from the nursery, or until he had passed the age when retrolental fibroplasia could develop.

#### RESULTS

Not one of the 126 babies in this study showed even the mildest manifestations of active retrolental fibroplasia.

Oxygen was given to even fewer babies and for even shorter periods of time than in the preceding two years of low oxygen administra-

#### ROYAL VICTORIA MONTREAL MATERNITY HOSPITAL

##### BABY'S OXYGEN RECORD

NAME Baby G. Born December 24, 10:10 pm Weight 1020 grams

Date	Time	Oxygen Concentration	Remarks
Dec 24,	10:15pm	38%	Colour good. Respiratory indrawing.
	11:00pm	38%	Mucous. Colour good. Indrawing still present.
Dec 25,	12:45am	35%	Less mucous. Active. Colour good. Respirations still laboured.
	2:15am	35%	Colour good. Breathing fairly regular.
	3:30am	35%	Breathing well. Colour good.
	6:30am	36%	Breathing well. Colour good.
	8:30am	27%	Colour good. Respirations regular.
	10:10am	26%	Colour good.
	11:00am	26%	Colour good. Oxygen discontinued.

Fig. 2.—Sample oxygen sheet. Entries are made routinely, at least once every two hours, day and night.



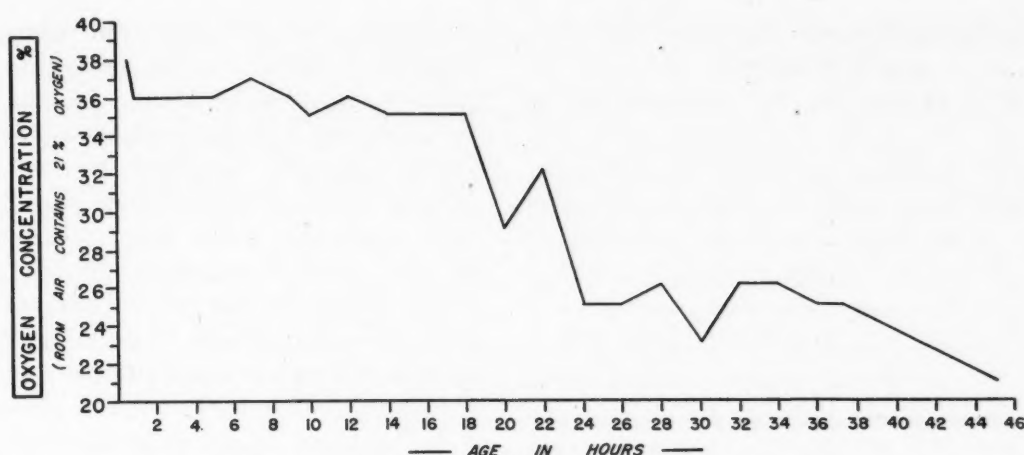


Fig. 3.—Oxygen history of a baby weighing 1500 g. at birth.

tion. Furthermore, the regular use of the oxygen analyzer\* assured that it was being given in lower concentrations. No increase in the mortality rate occurred (24.5% at the Women's Pavilion in 1952 and 1953; 22.3% in 1955) and no adverse effects on the babies' general development could be noted.

Thirty-two of the 126 babies received no oxygen, and in the case of another 44 babies the oxygen was discontinued during the first 24 hours of life.

Only three babies required oxygen for longer than eight days. One was an infant with cyanotic congenital heart disease weighing 1170 g. at birth. He died at the age of nine weeks, in spite of receiving higher than usual concentrations of oxygen (generally between 40 and 50%). The fundi remained normal prior to death. The other two babies were amongst our smallest. They weighed 720 g. and 975 g. at birth, and received oxygen for 13 and 19 days respectively. During the first four days of life, oxygen concentrations were kept between 30 and 40%, but afterwards extremely low concentrations, between 22 and 26%, were effective (Fig. 4). It was in the control and maintenance of these lower concentrations that the more sensitive Rotameter flowmeter† was of great value.

Five other babies weighing less than 1000 g. at birth received oxygen in similarly low concentrations, for 2, 4, 5, 6 and 7 days respectively.

## DISCUSSION

Most doctors now accept and follow certain fundamental practices governing administration of oxygen to premature babies. These are: (a) that oxygen should never be given as a routine measure, but should be administered only when there are clinical indications for its use; (b) that it should then be used in the lowest concentrations and for the shortest periods consistent with the baby's needs; (c) that the chief indica-

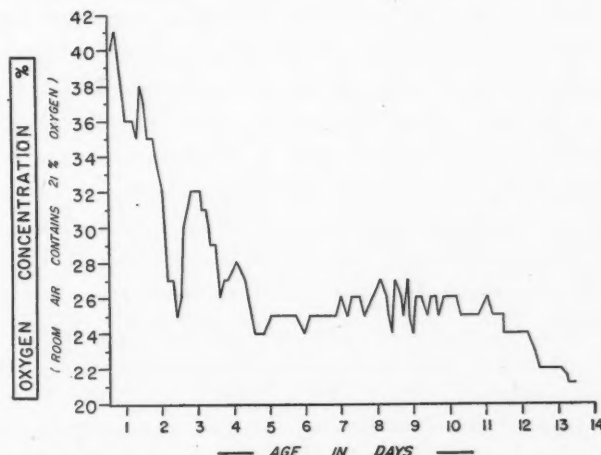


Fig. 4.—Oxygen history of a baby weighing 975 g. at birth.

tions for oxygen therapy are cyanosis and respiratory distress, and most particularly that periodic or irregular respiration *per se* is not an indication. And yet this is not enough. It is precisely when these principles alone are followed that sporadic cases continue to occur. Among the chief reasons for these continuing cases are:

1. Failure to use an oxygen analyzer regularly and at sufficiently frequent intervals. (We recommend that it be used not less than once

\*Analyzers that are accurate and simple to use are manufactured by Arnold O. Beckman, Inc., 1020 Mission St., South Pasadena, California, and by Medical Instruments Research Associates, 2656 North Pasadena Avenue, Los Angeles, California.

†Rotameter Manufacturing Co. Ltd., 602 Purley Way, Croydon, England. Canadian agent: J. L. McDougall, 1545 McGregor St., Montreal.

every two hours, day and night, and more frequently after initiating oxygen, changing its rate of flow, or opening the incubator lid or sleeves).

2. Failure to recognize that concentrations higher than 35 to 40% are only exceptionally required. In most instances, if oxygen want is not relieved by 40% oxygen, higher concentrations will rarely bring further improvement.

3. The all-too-prevalent impression gained from the current literature that concentrations below 40% are always safe. The only safe and correct approach is that of the lowest possible concentration for the shortest period of time.

4. Two fallacious concepts: (a) that oxygen is only one of several etiological factors and that, because of other causes as yet unknown, sporadic cases must be expected even with the best of care; (b) that, in some cases, prevention of the disease may not be compatible with survival in sick babies or very small babies requiring oxygen for a long period of time. These provide excuses for sporadic cases and hinder the application of better methods of oxygen control.

Some centres have adopted the use of a mixture of 40% oxygen and 60% nitrogen for supply to the incubators. The use of such a mixture does not absolve one from the necessity of making frequent oxygen analyses and from reducing and discontinuing oxygen as early as possible. Retroental fibroplasia can be produced in both animals and humans by exposure to concentrations of oxygen lower than 40%.<sup>3-5</sup> The method has the disadvantage that, while 40% is usually a sufficient maximum, infants may have apnoeic spells when adequate blood oxygenation should be restored as quickly as possible by the use of higher concentrations for short periods. Some infants with severe respiratory distress or cyanotic congenital heart disease may also require higher concentrations. The method may, however, lessen the danger of RLF in nurseries where a shortage of trained personnel hampers more meticulous control of oxygen, provided that it does not instil a false sense of security.

Automatic metering devices, which are supposed to deliver set concentrations of oxygen, have also been described, but are not yet sufficiently accurate to displace the oxygen analyzer.

If further blindness from this disease is to be eliminated, public health authorities and hospital licensing bodies should require the measuring and recording of oxygen concentrations at stated minimum intervals (by means of an oxygen analyzer), in the same way that potentially toxic and lethal drugs must be charted. By this means, excessively high concentrations could no longer be given unknowingly. This requirement could also be added to the "Standards for Hospital Accreditation" of the Joint Commission on Accreditation of Hospitals.

Compulsory reporting of cases should be instituted, as has been done in New York State,<sup>6</sup> and the methods of oxygen control in the hospital concerned investigated.

Finally, complete prevention can be accomplished only with the aid of properly trained nurses, since the responsibility for readjusting oxygen concentrations during the day, in accordance with changes in the babies' needs, devolves primarily on them. Medical students and nurses-in-training should be made more cognizant of this important problem.

#### SUMMARY

The continuing problem of unnecessary blindness from retroental fibroplasia has been stressed. One hundred and twenty-six premature babies, weighing 4 lb. or less at birth, have had their oxygen carefully controlled. No cases with even the mildest manifestations of the disease occurred. There was no increase in the mortality rate and no adverse effects on the babies' general development. It is our belief that retroental fibroplasia is completely preventable. Suggestions for preventive public health measures have been made. General recommendations for the control of oxygen therapy in premature babies are appended.

#### APPENDIX

##### *Recommendations for the control of oxygen therapy in premature babies.*

*Delivery room:* No restriction is necessary in the use of oxygen for resuscitation. The oxygen here should be moistened wherever possible.

*Nursery:* (1) Any infant requiring oxygen should be nursed in an environment which can be kept as constant as possible. It has been shown that semi-open incubators allow considerable fluctuation of oxygen concentrations at constant flow rates.<sup>7</sup> Wherever possible, a closed-circuit model should be used.

2. If oxygen is required, a record sheet (Fig. 2) should be kept. This should have space for the baby's name, date and hour of the oxygen analysis, the oxygen



concentration as determined by the oxygen analyzer, the flow rate in litres or c.c. per minute, and remarks about the baby's colour and respiratory activity. Entries should be made at least once every two hours, day and night. After the initiation of oxygen, and after any alteration in its flow rate, analyses should be made more frequently, until steady values are obtained.

3. There is no longer any excuse for a hospital which has an incubator not to provide an analyzer, specifically allocated to the nursery so that it is always available. The average cost of rearing one premature infant has been estimated at \$400.<sup>8</sup> The price of an oxygen analyzer for the entire nursery is less than half this figure, and the instrument will last an indefinite time with proper use. The time required to measure and chart an oxygen concentration is about 10 seconds—less than that required to take and record a patient's pulse or temperature.

4. Oxygen should never be given as a routine measure, but only in the presence of definite indications, which have already been mentioned. When used, it should not be left running over 35 to 40% without specific directions from the physician in charge of the case, who must then either visit the baby more frequently to be sure such concentrations are still necessary, or leave orders with the nursing staff to reduce the oxygen as quickly as possible. Concentrations below 30% are usually sufficient to relieve cyanosis and concentrations as low as 22 to 26% are often effective, especially in small babies needing oxygen over a long period of time. Size alone, however, should be no deterrent to discontinuing oxygen. Two of our smallest babies did well out of oxygen when weighing less than 665 g.

5. To control and maintain the lower concentrations effectively, we recommend a more sensitive flowmeter such as the Rotameter, which allows changes in flowrate of tenths of a litre.

6. Oxygen should be discontinued as soon as possible. It is preferable to stop and then restart, if necessary. In some cases, oxygen need only be given intermittently. There is no danger in rapid withdrawal of oxygen provided it has been maintained at the levels under consideration here. Rapid weaning is preferable to maintaining a baby in oxygen for several more days for the sake of a gradual withdrawal. However, if a baby can withstand sudden withdrawal from a 40% concentration, it suggests that he probably could have tolerated a lower concentration earlier.

7. The recommendation that oxygen should be used in treating the active disease has not been upheld. The disease has developed while babies were still in oxygen, and many cases have become worse in spite of treatment with oxygen. The good results reported by those who advised such treatment may be due to the tendency of RLF to undergo spontaneous arrest or regression in approximately 70% of cases. We believe that by the time the first vasoproliferative fundus changes are seen (usually between one and seven weeks of age) the ultimate fate of the eye has already been determined and that any subsequent changes in the oxygen environment will have little or no effect on the final result. The critical period for oxygen control is during the earliest days of the premature baby's life.

8. Some incubators designed before the dangers of oxygen toxicity were known have an attachment for providing a supersaturated environment, which is dependent on an inflow of oxygen. If supersaturation is desired in cases not needing oxygen, a compressed air pump rather than the oxygen inflow mechanism should be used.

9. The active co-operation of the nursing staff is of the utmost importance in a successful RLF control program. Since the baby's oxygen needs vary during the day, the control of the oxygen must be under constant surveillance. The nursing staff must have the necessary training and authority to reduce the oxygen when it is apparent that the baby can get along with less, or to increase it if necessary.

10. Careful ophthalmoscopic examination of the fundi should be carried out shortly before the baby's discharge from the nursery, by which time the early manifestations of the acute phase will have appeared if the disease is going to develop. This will ensure that no errors are being made in the use of oxygen.

All paediatricians and other physicians now know that oxygen in high concentrations is dangerous, but they often do not know how easy it is to reach dangerous concentrations with modern incubators. The new incubators are reaching small hospitals faster than the knowledge of the correct use of these machines. No hospital should order an incubator for the first time without ordering an oxygen analyzer as well.

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#### RÉSUMÉ

La fibroplasie rétrolenticulaire a été complètement éliminée d'un groupe de 126 nourrissons pesant 4 lbs. (1800 grammes) ou moins à la naissance. L'oxygène thérapeutique ne fut employé qu'à la ressuscitation, et dans les quatre indications suivantes: la cyanose d'anoxémie artérielle, les troubles respiratoires, la pâleur ou la léthargie qui peuvent suivre l'administration d'oxygène ou la tétée. Sauf dans les cas exceptionnels, la concentration n'excéda pas 40% et fut vérifiée à maintes reprises afin de ne pas excéder cette limite. L'examen ophtalmoscopique fut pratiqué chaque semaine. En dépit de la diminution considérable dans l'administration d'oxygène, aucun effet fâcheux ne fut noté dans le développement de ces enfants. L'emploi du compteur ROTAMETER (marque déposée) s'est avéré fort utile dans la détermination exacte des basses concentrations. Il découle de ces constatations que l'oxygène ne doit être administré que pour des indications cliniques bien déterminées, en concentrations aussi basses que le permettent ces indications, et pour des périodes de temps aussi brèves que possible. (Le risque de F.R.L. ne disparaît pas nécessairement à une concentration inférieure à 40%.) La prévention de cette infirmité peut maintenant être exercée à un tel degré que les autorités d'hygiène publique devraient l'inclure parmi les autres mesures de médecine préventive. Une liste de recommandations facilitant l'application du contrôle de l'oxygène termine cet article.

M.R.D.

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## THE PRACTICAL MANAGEMENT OF CARDIAC ARREST\*

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THIS PAPER is presented with the belief that surgeons likely to read this are more interested in the actual method of preventing and treating cardiac arrest than in an academic discussion of the subject.

The term "cardiac arrest" refers to arrest of the circulation under two circumstances: (1) ventricular fibrillation; (2) cardiac standstill. In "standstill" the heart is quite motionless and there is no electrical activity to be seen on the electrocardiogram. In ventricular fibrillation, due to the asynchronous contraction of groups of muscle fibres, the heart exhibits a writhing, squirming action, which is represented by an irregular, continuous wave motion in the electrocardiogram. In neither of these conditions does the heart expel blood and thus the circulation is completely arrested.

Aside from mentioning some of the more important physiological principles, no attempt will be made to discuss the problems of etiology or incidence, which are excellently reviewed elsewhere.<sup>1-9, 13, 14</sup> Emphasis will be given to a description, with illustrations of the actual technique of management, of cardiac arrest.

### SOME PHYSIOLOGICAL PRINCIPLES

1. First a word about *oxygen* and hypoxia in surgery. Most classifications of the etiology of cardiac arrest include such major factors as: hypoxia, vasovagal stimulation, drugs and anaesthetics, hypercapnia and manipulation of the heart. Although hypoxia is sometimes the sole apparent cause of arrest, very frequently it is an important accessory factor acting in combination with any of the other factors. Thus, if arrest follows the use of a drug or special anaesthetic, one usually finds associated hypoxia. When the arrest is considered vasovagal in origin, such as that which occurs during the passing of an endotracheal tube, one should be suspicious of a coincident hypoxic state.

One of the more important surgical concepts developed in the past decade is the fact that surgeons and anaesthetists are unable to recognize significant degrees of hypoxia in their patients during surgery. Changes in the patient's blood pressure, pulse or colour and darkening of the blood in the operative field are late signs indicating a severe degree of hypoxia. Milliken oximeter studies of arterial oxygen saturation during surgical operations were carried out by Kergin<sup>11</sup> and others. They showed that the anaesthetist and the surgeon may be quite happy about the progress of an operation even though the patient's arterial oxygen saturation is running as low as 80 to 85%. Although not serious for a brief period, if this state is prolonged it becomes just as dangerous as a more severe form of oxygen lack and renders the heart irritable and sensitive to stimuli.

The newer techniques of anaesthesia, using curare and allied drugs, are particularly dangerous, for the amount of anaesthetic required to produce relaxation will also inhibit respiratory mechanisms sufficiently to produce hypoventilation and hypoxia. Aware of his inability to recognize hypoxia, the anaesthetist should constantly strive to maintain full oxygenation by assisting respirations with positive pressure oxygen.

There are two further sources of hypoxia during the induction of anaesthesia. Immediately after the injection of enough thiopentone (Pentothal) to produce rapid anaesthesia there is definite fall in arterial oxygen saturation. The patient is therefore hypoxic from the moment of injection until the mask is put in place and oxygen supplied. Secondly, pulmonary ventilation is usually decreased during insertion of the endotracheal tube and it has been suggested that, as a guide, the anaesthetist might hold his breath during the entire period of intubation.

2. A great deal has been written about the part that *carbon dioxide* plays in cardiac arrest. It is possible with modern anaesthetics to have inadequate respirations with a build-up of carbon dioxide in the blood (hypercapnia) while the arterial oxygen saturation remains relatively unchanged. Although this in itself produces irritability of the heart, it has been found that suddenly reducing the accumulated carbon dioxide by vigorous ventilation is sometimes associated with the development of cardiac arrest.<sup>6</sup>

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Many of the cases of cardiac arrest in general surgery occur during the induction of the anaesthetic or as the surgeon begins to close the abdomen. For instance, when the surgeon announces that he is ready to close the abdomen, more relaxant is usually given and positive pressure respirations are increased. If there had been some hypercapnia from inadequate respiratory exchange before this time, the excess CO<sub>2</sub> would suddenly be blown off, setting the stage for cardiac arrest.

3. Hypoxia of the heart and other organs may also result from *decreased cardiac output* and hypotension secondary to excessive manipulation or haemorrhage. It is the surgeon's responsibility to prevent this situation arising and, if it occurs, to correct it immediately. This is not only a demand on his technical skill but his preparation for operation should include an adequate supply of whole blood and a satisfactory means of rapid transfusion. In all major surgery a cut-down or stab intravenous with a 17-gauge needle is advisable. Some device should be available so that the blood may be pumped rapidly in an emergency.

In the past, the term "chronic shock" has been applied to patients who, secondary to chronic debilitating illnesses, developed a low circulating blood volume.<sup>16</sup> It is seen more commonly in the aged and can be present even though the haemoglobin and serum protein levels are normal. If subjected to surgery without preoperative restoration of his blood volume, this patient has a marked tendency to develop shock. Under average circumstances the patient's blood volume tends to be 50 c.c. below normal for every pound of weight lost in the previous nine months.

#### LENGTH OF TIME AVAILABLE

How long can the circulation be suspended without permanent severe damage to either the heart or the brain? Although the brain is considered somewhat more tolerant of hypoxia than the heart, it is true that occasionally where cardiac resuscitation was started late the patient has survived but shown severe cerebral damage. Actually the brain and heart exhibit approximately equal sensitivity to hypoxia, and four minutes is usually considered as the limit before permanent damage occurs.<sup>10, 14</sup>

This time limit is influenced by several factors. Younger children and infants tolerate hy-

poxia longer. Of course, a diseased heart will succumb before a normal one.

Another important concept is the cumulative effect of various mild episodes of hypoxia. During a surgical operation these may occur as stated above, with the induction of anaesthesia, intubation, haemorrhage or perhaps as a result of accidental bronchospasm. A heart that has been exposed to repeated periods of hypoxia during an operation will not tolerate as long a period of arrest as the heart of an individual whose blood has been fully oxygenated until the moment of arrest.

#### REPORT OF CASES OF CARDIAC ARREST

The authors have analyzed 34 cases of cardiac arrest in 600 heart operations at the Toronto General Hospital. Twenty-six were cases of ventricular fibrillation and of these eight patients died in the operating room, nine died one hour to ten days after the procedure and nine survived permanently. It was significant that electrical defibrillation successfully reverted each of these hearts to temporary standstill at

TABLE I.—RESULTS OF 34 CASES OF ARREST

Cases	No.	Recovery from operation	Complete recovery
Ventricular fibrillation .	26	18 (70%)	9 (33%)
Standstill . . . . .	8	8 (100%)	3 (37%)

least once. In eight of the 34 cases there was cardiac standstill rather than ventricular fibrillation. In this group there were no operative deaths but there were five late deaths and three permanent survivals.

In addition to these 34 cases of cardiac arrest there were eight other operative deaths which were classified separately as either fatal haemorrhage or acute heart failure.

The high incidence of recovery in ventricular fibrillation is felt to be attributable to the prompt use of the electrical defibrillator (cf.<sup>3, 8</sup>).

#### DISCUSSION

The authors' experience with cardiac arrest has occurred mainly during cardiovascular surgery on patients with diseased hearts. In these cases cardiac arrest has usually developed during manipulation of the heart and, because

\*Included in this series are a variety of procedures including insertion of plastic valves; open heart surgery with hypothermia, etc.

of the pre-existing cardiac disease, ventricular fibrillation was the dominant feature. In general surgery the majority of patients will be in cardiac standstill and will have a relatively normal cardiovascular system. Prompt action and good technique should result in the resuscitation and survival of the vast majority of these.

Before surgeons can hope to obtain accurate statistics and better understanding of cardiac arrest, there must be a clearer and more comprehensive definition of terms. Since we all die when heart action ceases, is this to be referred to as cardiac arrest? For example, in overwhelming toxæmia or asphyxia or coronary thrombosis the heart becomes incompetent and unable to function. This terminates in either cardiac standstill or ventricular fibrillation. Now it is quite possible that one may be operating upon a patient whose heart is very near the terminal stage of disease or incompetence. In such a situation the anæsthetic and operation may cause a slow, gradual decline of heart action with falling blood pressure over a period of 10 to 60 minutes until the heart finally stops. Should this patient, with a terminally diseased heart that has gradually succumbed to the added strain of surgery and anæsthesia, be classified as a case of cardiac arrest? One would not expect to resuscitate such a heart. The writers feel that this is quite a different situation from the heart that one moment is beating adequately and then suddenly or over a period of several minutes stops beating. The authors suggest that the term "cardiac incompetence" be used to describe this terminally diseased heart that slowly fails and cannot be resuscitated.

Massive, uncontrollable hæmorrhage, which is inadequately treated by transfusion, may also result in operative death. Again, without adequate blood replacement, resuscitation is obviously impossible. Under such circumstances it is doubtful that such a death should be labelled cardiac arrest. Rather, cardiac arrest should imply the decline of heart action over a brief period of minutes where the cardiac state is reversible and resuscitation is possible.

#### TREATMENT

##### *Prophylaxis*

One of the most important forms of prophylaxis is to make sure that the entire surgical

team is fully aware of the difficulty in recognizing hypoxia and the dangers of subclinical hypoxia during surgery.

##### *The Resuscitation Tray*

About one case of cardiac arrest in six, exclusive of cardiac surgery, does not occur in the operating room, but in the plaster room or cystoscopic room or on the ward. A resuscitation tray should be available for use both in the operating room and outside. A knife should be available which will be sufficient to allow entry into the chest, in order to commence massage. The simplest resuscitation equipment is a sterile scalpel in a test tube hanging on the wall along with a whistle.

Accessory instruments and drugs will be needed in order to provide the best in cardiac resuscitation. The cardiac resuscitation tray should be kept sterile and well-marked, and it is worth while to suggest that it be wrapped in a red cloth. Thus it may be found in a hurry, even by a person who is not familiar with surroundings. A bare minimum of instruments should be on this tray. The following are quite adequate:

- |                                    |                       |
|------------------------------------|-----------------------|
| 1 scalpel                          | 1 medium Mayo needle  |
| 1 pair of scissors                 | 1 needle driver       |
| 6 small forceps                    | 5 21-gauge needles    |
| 6 towel clips                      | 4 50-c.c. beakers     |
| 1 long Kelly forceps               | 6 abdominal sponges   |
| 1 Adson thumb forceps              | 2 small towels        |
| 1 10" plain thumb forceps          | 1 Deevor retractor    |
| 1 self-retaining rib retractor     | 1 large Mayo needle   |
| 3 10-c.c. syringes for (Luer-lock) | (1 procaine 1%        |
|                                    | 1 calc. chloride 10%  |
|                                    | 1 adrenaline 1/10,000 |

On top of the tray, and attached to it, an unsterile bundle containing:

- 2 10-c.c. ampoules of calcium chloride, 10%
- 1 small bottle of 1% procaine
- 2 ampoules epinephrine (adrenaline) 1/1000
- 1 small bottle of saline
- 2 ampoules of 1 chromic catgut
- 1 laryngoscope
- 2 sizes of endotracheal catheters (inflatable cuff)\*

The laryngoscope and endotracheal catheters should be included in the unsterile bundle if the tray is not to be kept near or in an operating theatre.

##### *Recognition of Cardiac Arrest*

A sudden absence of peripheral pulses and lack of blood pressure are the commonest indi-





Fig. 1.—Rapid incision of left chest just below the nipple. The 4th or 5th space is opened by cutting the intercostal muscles. The ribs are spread manually and massage is quickly started.

cations of cardiac arrest. Of course, in thoracic surgery, an electrocardiograph may be in operation. When the surgeon has the chest open, direct observation of the heart action is most reliable.

With absence of pulse or blood pressure, one will naturally correlate this observation with the colour of the patient or the colour of the blood.

There is one important concept concerning recognition. Cardiac arrest may occur during the best regulated operation. The surgeon and anaesthetist must realize that it is not necessarily an indication of inferior workmanship. At the first sign of absent blood pressure and pulse, the anaesthetist must quickly announce to the surgeon his fear that cardiac arrest has occurred and that he is confirming this by further observation of pulse or blood pressure. During the 10 or 15 seconds that the anaesthetist is checking his observations, the surgeon may simultaneously confirm the diagnosis by palpating a major artery (i.e. the aorta if he is working in the abdomen). He mobilizes his thoughts

and plans his next move, should resuscitation be necessary. A surgeon will accept an occasional false alarm because the anaesthetist's prompt warning provides him with the maximum time, and thus the greatest chance of resuscitation.

#### *Technique*

##### *(a) Airway and Oxygen.*

With cardiac arrest, respirations cease and it is essential to have a free airway with positive pressure oxygen. It is the first and immediate duty of the anaesthetist to establish either pharyngeal or intratracheal airway and to rapidly obtain a source of oxygen. Of course an endotracheal tube and anaesthetic bag for positive pressure is ideal. Temporary emergency measures such as mouth-to-mouth breathing may be effective while equipment is being obtained. Mouth-to-mouth breathing is particularly effective in children.

##### *(b) Exposure of the Heart.*

*(i) Cardiac arrest when neither the abdomen nor the chest is open.*—Under these conditions the left anterior chest should be entered through



Fig. 2



Fig. 3

Fig. 2.—After brief massage with the pericardium intact, more efficient massage is obtained by widely opening the pericardial sac, as shown in diagram. Fig. 3.—Hand within widely opened pericardial sac, compressing heart rhythmically, so that a blood pressure of over 65 mm. Hg is obtained with constricted pupils.

the fourth or fifth space, using an incision starting about an inch and a half from the lateral border of the sternum and extending around to the mid-axillary line (Fig. 1). In most instances, preparation of the skin will not be feasible. Be careful in going through the parietal pleura that you do not cut the lung. Make a small opening first, which will allow air to enter the pleural cavity. The lungs will then retract and the danger of injury to the lung is remote. The internal mammary artery lies in the medial end of this incision. It is best to avoid cutting it, although if it is cut this is not serious. It may cause some bleeding, which is sometimes difficult to control, but a firm suture later will usually suffice. The hand should be inserted through the chest after quickly prying open the ribs and grasping the heart, without opening the pericardial cavity, and massage commenced. The ribs on either side of the open space will press on the surgeon's wrist, but this is acceptable and may be corrected and better vision obtained in a few minutes, if necessary, by the insertion of a self-retaining retractor or by an assistant retracting the upper rib.

Many of the hearts will commence beating within a minute or two of the first massage. However, if the heart does not start beating after about two minutes of massage, and if

proper exposure has been obtained by rib retractors, then one may stop massage for a few seconds and rapidly open the pericardium (Figs. 2 and 3). This allows more effective massage.

This is sometimes difficult to do because the pericardium is very tightly wrapped around the heart and if the heart is dilated it will be even more tight than normal. The best method of opening the pericardium is to use the Adson thumb forceps or some form of thumb forceps with teeth. The pericardium is picked up anteriorly to the phrenic nerve and cut liberally with scissors. Once there is a cut one or two inches (2.5-5 cm.) long in the pericardium, insert two fingers under the pericardium and lift it up away from the heart; then the incision may be continued without danger to the heart or coronary vessels. The pericardium should be cut liberally, as far above and below as is possible. (It must be adequately retracted.) If the pericardium is partially intact, when the hand is inserted between pericardium and heart, the resulting limited space will prevent adequate filling of the heart in diastole during massage.

(ii) *Cardiac arrest during abdominal surgery.*—Perhaps one of the commonest problems that will face a general surgeon is the case of a pa-





Fig. 4.—Cardiac arrest during abdominal operation. Brief massage through intact diaphragm. If the heart does not start within a minute, the chest should be quickly opened to allow better massage.

tient with an abdominal incision who develops cardiac arrest. In these circumstances we believe that the heart should be massaged immediately through the intact diaphragm (Fig. 4). One cannot grasp the heart satisfactorily in this position, but it may be compressed rhythmically against the sternum. Stop the anaesthetic and oxygenate the lungs.

If the heart fails to respond within one minute of cardiac massage, an assistant should open the left chest while massage is being carried out below, in order to get a better exposure of the heart. If no competent assistant is present, the surgeon will obviously have to leave the abdomen and open the chest as rapidly as possible. The chest exposure will allow him to remove the pericardium; allow more adequate massage; and facilitate the intracardiac or intra-aortic injection of drugs.

In small children and infants quite adequate cardiac massage may be carried out through an opening in the diaphragm.

#### *Method of Cardiac Massage*

The accompanying illustrations demonstrate the position of the hand. The best and most forceful massage is obtained with the right

hand (Fig. 5) with the apex lying between thumb and index finger and the heart squeezed as well as compressed against the vertebral bodies in a manner which forces the blood into the base of the heart and into the great vessels. The left hand (Fig. 6) may be just as effective and in each case the manoeuvre includes the compression of the heart against the vertebral bodies.

Cardiac massage must be forceful and at the fastest rate that one can obtain diastolic filling. This is usually around 60 to 70 per minute in a heart with good tone. It is important from the onset to check your technique of massage with regard to position of the hand, rate and force of massage by periodic blood pressure recordings. Under ordinary circumstances, blood pressure should be easily recorded with a systolic pressure between 70 and 130 mm. Hg on the blood pressure cuff during massage.

The key to adequate cardiac massage is an understanding of heart muscle tone. Perhaps the best way to appreciate this is to realize that the ventricles are potential cavities; if the heart muscles are in good tone they have a definite tendency to produce a cavity. This may actually suck the blood into the ventricle

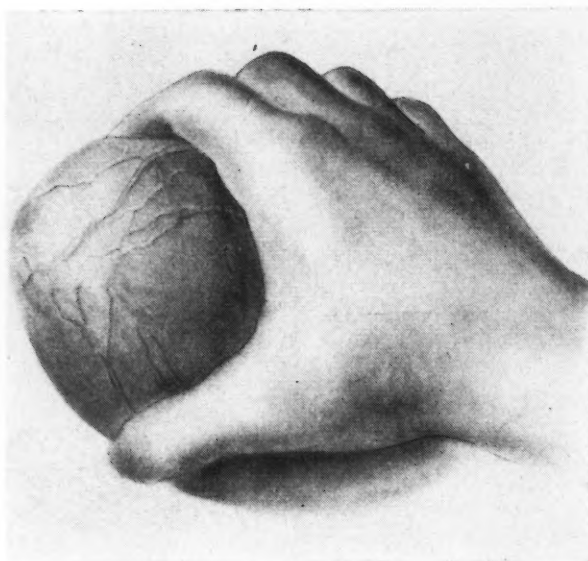


Fig. 5

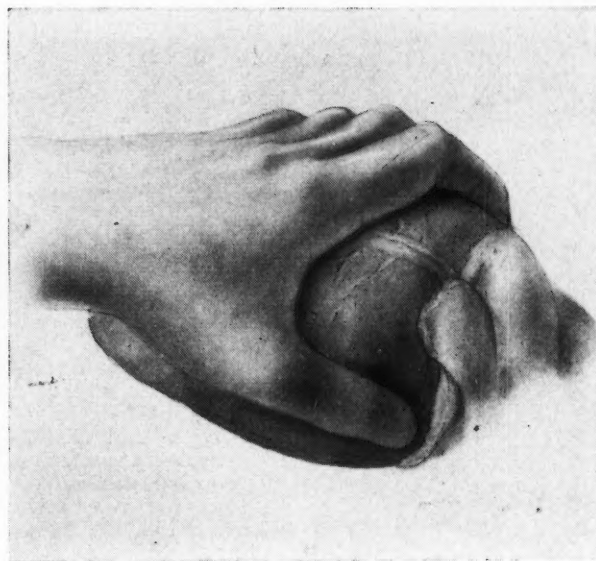


Fig. 6

Fig. 5.—Left thoracotomy and right hand applied with apex of heart lying between thumb and index finger. Heart is squeezed and compressed against vertebral column, with an action that forces blood into the great vessels. Fig. 6.—Left chest opened. Massage with the left hand in a large adult heart is most efficiently carried out as shown. The heart is squeezed and at the same time compressed against the vertebral column.

from the atrium, producing more adequate and more rapid filling. Conversely, in heart muscle without tone, the ventricle walls are inert and lax and collapsed. In this condition the ventricle is slowly filled by blood, relying only on what pressure there may be in the atrium to force the blood ahead.

The assessment of muscle tone by palpation, and the ability to decide whether the heart is filling during the relaxation phase of massage, comes with experience. Such experience may be gained with an experimental animal. The tone is a *sine qua non*, in spite of careful technique, rate and force of massage. Its actual efficiency is determined by the cardiac output and pressure obtained, which in turn depends upon muscle tone.

#### *The Use of Drugs*

Drugs are primarily used to improve the myocardial muscle tone, which in turn improves the diastolic filling of the heart during massage, which results in more effective cardiac massage, as measured by the blood pressure. They should not be used as an aid to cardiac resuscitation under ordinary circumstances until full aeration of the lung and good cardiac massage for five minutes has failed to restore cardiac muscle tone. The best of cardiac massage will not produce a satisfactory cardiac output unless adequate muscle tone is present. A heart in standstill will never be restored to

spontaneous rhythm unless the myocardium is of good muscle tone. It is also quite impossible to defibrillate a heart that is in ventricular fibrillation unless there is good myocardial tone and vigorous ventricular fibrillation.

If good massage and aeration for about five minutes has not produced this state of affairs, then one of two drugs is recommended. One should inject either 1 to 5 c.c. of 10% calcium chloride, or 0.5 to 5 c.c. of adrenaline 1:10,000. The amount should depend on the size of the patient. The initial dose of adrenaline should not be over 2 c.c. in an adult.

These solutions are best injected using a 10-c.c. syringe and a 21-gauge needle. A needle any smaller causes a delay in aspirating blood to determine the position of the needle, and if it is any larger it has a tendency to cause local bleeding from the needle hole. A suitable area in the lateral aspect of the left ventricle, as far away from a major branch of the coronary artery as possible, is selected, and on aspirating bright red blood the solution is injected rapidly, making sure that the needle maintains its exact position to ensure against possible intramural injection. The heart may be forcibly steadied with the left hand during injection to ensure this. Vigorous massage is carried on up to the very moment of injection, and immediately after injection massage is instituted again to minimize the period of arrested circulation caused by this manoeuvre.



The authors' personal opinion is that adrenaline is more effective but it does have a tendency to produce some increased irritability of the heart. Calcium chloride is slightly less effective (unless one is dealing with previous massive hæmorrhage and transfusion) but does not contribute to this increased irritability. We would suggest that calcium chloride be injected first, followed by a further five minutes of cardiac massage. If the tone has not returned, then follow this with an injection of adrenaline and further massage.

The only other drug in common use for intracardiac injection is 1% procaine solution. Procaine is much less useful as an aid to resuscitation than was previously thought. It does reduce irritability and reduces the tendency to develop ventricular fibrillation, but it also has a tendency to produce a loss of muscle tone if too much is used, and that is a bad feature. Occasionally, when a heart is obviously far too irritable and prone to develop ventricular fibrillation, 2 to 5 c.c. of intracardiac procaine is indicated.

No-one knows exactly what quantities of intracardiac drugs should be used. Over a period of 1 hour's cardiac massage it may be necessary to use a total of 20 c.c. of 10% calcium chloride and 20 c.c. of 1:10,000 adrenaline.

#### *Occlusion of the Thoracic Aorta*

When the initial period of massage, followed by the use of drugs, has failed to restore heart action, and when cardiac muscle tone and adequate blood pressure (over 65 mm. Hg) have not been obtained, it is a worth-while manoeuvre to very quickly free the aorta just distal to the left subclavian artery by blunt dissection through the mediastinal pleura and apply a long Kelly clamp to the aorta. The entire aorta does not need to be dissected free to accomplish this. The cardiac massage then forces the blood into a restricted vascular bed and increases the coronary filling. Such a clamp may be left in place for periods of five minutes without ill effect. If cardiac action has been restored with the clamp in place, it should be removed very slowly.

#### *How long should Cardiac Massage be Maintained?*

Cases have been reported of the restoration of normal cardiac function after over eight

hours' cardiac arrest.<sup>15</sup> In the authors' series of 34 cases, there were periods of arrest varying from 20 minutes to 1 hour and 10 minutes. One should, theoretically, continue active cardiac massage until signs of irreversibility and true death have developed. When the pupils have become widely dilated and show no response to increased vigour of cardiac massage in the absence of any drug effect, it is usually considered time to desist. Inability to induce cardiac muscle tone or obtain a recordable blood pressure during vigorous massage, along with dilated pupils and non-responsiveness, is a guide to abandonment of resuscitation efforts.

The authors recently encountered a cardiac arrest in a patient with a very diseased myocardium and coronary tree. As an index of adequate cardiac massage, the patient could be allowed out of anaesthesia 3 hours and 15 minutes after his heart had stopped, and he would respond intelligently to questions and move about vigorously. Although cardiac massage had maintained life for this period of time, it proved impossible to restore normal heart action and massage was eventually stopped.

It is encouraging to realize that most of the cases of cardiac arrest encountered in general surgery will be in the form of cardiac standstill and so will usually respond immediately to cardiac massage by return of heart action.

#### *Ventricular Fibrillation and Electrical Defibrillation*

Although, as stated above, in general surgery one will most often encounter cardiac standstill, there will be a certain percentage of cases of ventricular fibrillation. Occasionally a heart in standstill after a period of massage will develop ventricular fibrillation. Occasionally a heart that is in ventricular fibrillation will spontaneously revert to sinus rhythm and commence beating normally with nothing more than good massage and improved coronary filling. The majority of instances of ventricular fibrillation, however, will not revert without electrical defibrillation. Thus, without an electrical defibrillator, a surgeon will be likely to lose all patients who develop ventricular fibrillation.

From the several articles that have been written with descriptions of ventricular fibrillation, it should be easily recognized. The heart appears to be squirming, like a very vigorous



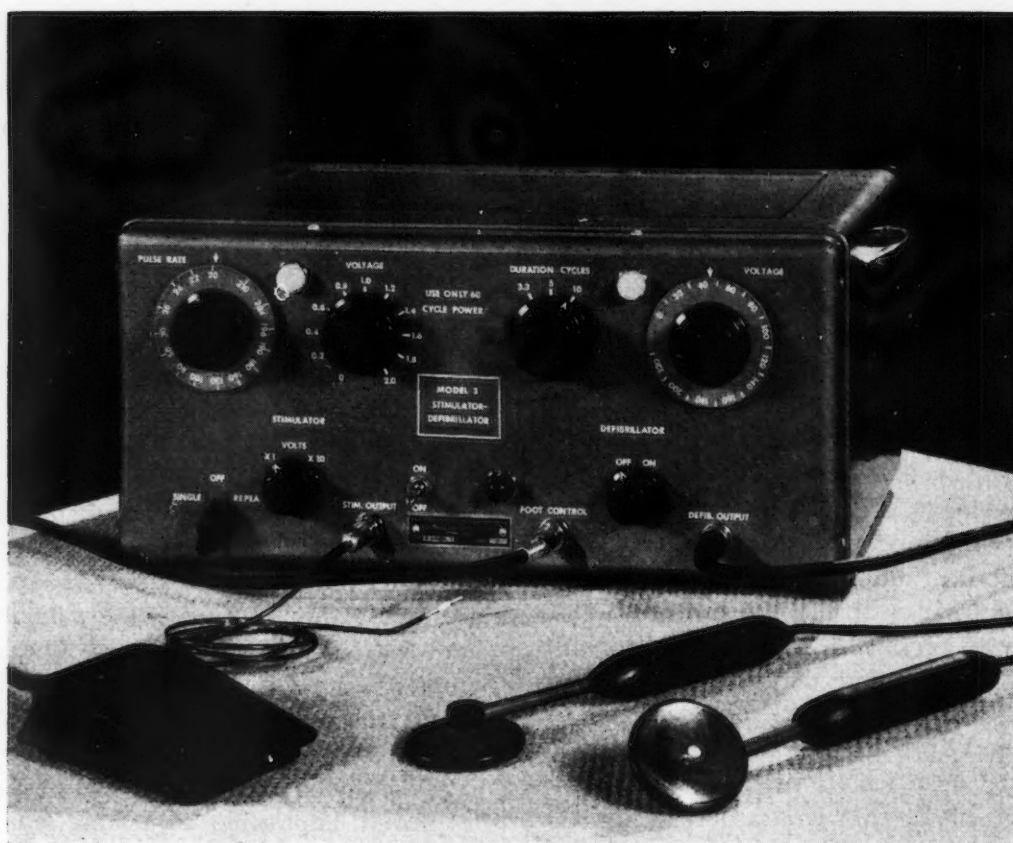


Fig. 7.—In ventricular fibrillation, spontaneous reversion to normal heart action by massage is infrequent. Most cases require the use of the electrical defibrillator. This model is an electrical stimulator as well, but simple models are available.

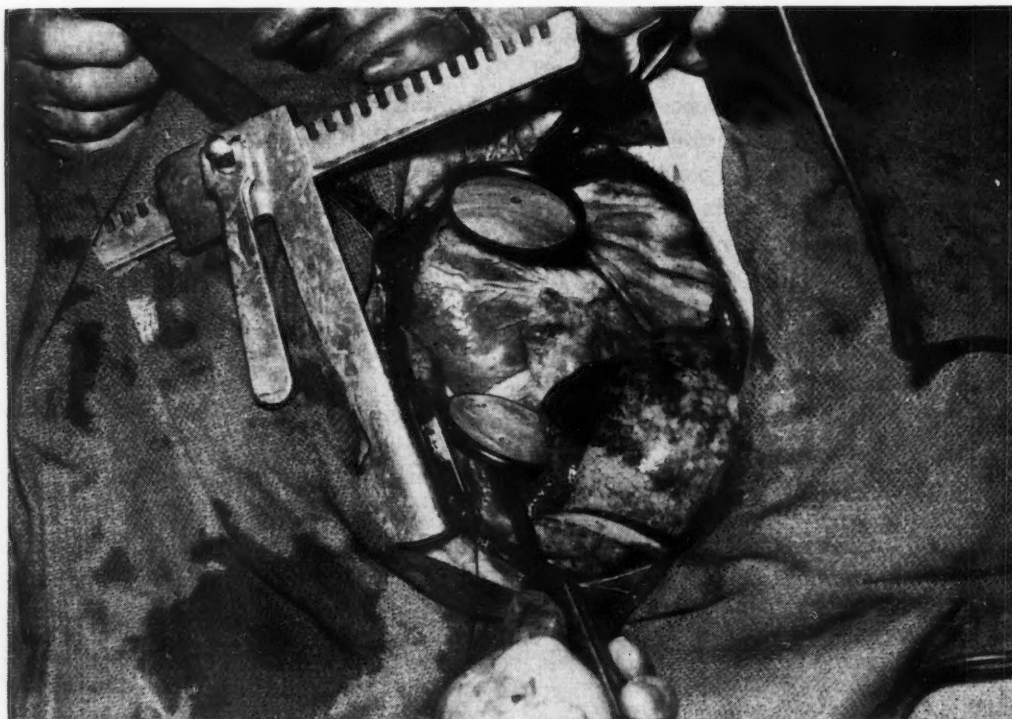


Fig. 8.—Electrodes are ready and moist with saline. The pericardium is widely opened to accommodate the electrodes.



Fig. 9.—Electrodes are placed on the heart, so that the greatest possible ventricular mass is between them. One electrode is placed near the apex of the heart.

bag of worms, with no expulsive beats, although very often the auricle is still beating.

In the case of ventricular fibrillation, the procedure is exactly as outlined for cardiac standstill. Massage must be instituted immediately and if the tone does not return within a few minutes of adequate massage and ventilation, intracardiac drugs may be injected. The heart muscle must be of good tone and the ventricular fibrillation very vigorous and easily palpated before electrical defibrillation is possible. Once this has been achieved, the defibrillating electrodes should be made ready and quickly put in place and a shocking current passed through the heart by means of the foot pedal.

#### *The Defibrillator*

Electrical defibrillation is not possible unless the defibrillating unit is applying the correct shocking current (Fig. 7). A current of over 1.7 amperes is required and voltage is of 170 to 220. There should be a device to ensure that the length of exposure to this electrical current

does not exceed 0.3 second. To use an electrical current off the wall outlet will in most cases prove inadequate. The electrical principles underlying the defibrillator have been described by Hopps.<sup>17</sup> There are two or three very adequate defibrillators being sold by commercial firms. The stimulator is of very little use surgically.

The defibrillator electrodes should be moistened with saline and applied firmly to the heart with as broad a surface of contact as possible. The largest possible ventricular mass should lie between the electrodes. One of the electrodes, preferably posteriorly placed, should extend close to the apex since this is the most difficult area to defibrillate (Figs. 8 and 9).

By means of a foot control, one shock should be passed through the heart and its results observed. In about four seconds it is possible to decide whether the heart has been defibrillated, and if one shock does not accomplish this it should be followed immediately by a series of three to five shocks in rapid succession. The electrodes should then be removed and



the heart observed. If normal expulsive beats do not return with this, cardiac massage should be restarted and once the muscle tone has reached its maximum the defibrillation technique should be repeated.

#### *Manually Assisted Heart Action*

When a heart in standstill suddenly commences to beat as a result of cardiac massage, it does not necessarily mean that the contractions are adequate to maintain circulation. This should be immediately assessed by blood pressure reading and following the size of the pupils. If the blood pressure is not recordable (namely, under 70 mm. Hg), it may be assumed that the resultant poor coronary filling will cause the heart to lapse into cardiac standstill.

A similar situation exists with ventricular fibrillation. When electrical defibrillation suddenly produces a normally beating heart, once again it must be tested to determine whether the beats are expulsive and circulation is adequate. Further confirmation of the type of heart beats is obtained by observation and gentle palpation of the heart.

If the heart has started to beat with evidence of inadequate cardiac output and this situation is allowed to exist for long, cardiac arrest will return. Under these circumstances, the systolic expulsion from the ventricle may be aided by gentle massaging in time with the heart beat. This is sometimes difficult to do if the heart starts beating rapidly and it may necessitate assisting every other beat. This must be done gently, for in an irritable heart this type of massage may precipitate ventricular fibrillation. This assisted massage may be stopped periodically and the blood pressure recorded until such time as the unassisted heart can maintain a reasonable blood pressure. If there is any evidence of this blood pressure not being maintained, there is a place here for further injection of calcium chloride or adrenaline into the left ventricle.

#### *Closure of Pericardium and Chest Wall*

After the heart action has been restored and adequate blood pressure maintained for several minutes, the pericardium should be partially closed with a curved intestinal catgut suture, leaving a space as large as a 25-cent piece for drainage and as a means of preventing cardiac tamponade. If there is any reason why the peri-

cardium should not or cannot be restored, it is not serious to leave the pericardium open, but it must be widely open so that the heart may dislocate and return freely into its natural position.

A red rubber drainage tube should be inserted through a stab wound, which is made in the seventh or eighth space. The patient will very likely be in the dorsal position, so that the incision will be made as far posteriorly as possible, ideally in the posterior axillary line. This should be attached to an underwater drainage bottle (but until this is ready the tube may be clamped). Interrupted double No. 1 chromic catgut sutures should be passed around the ribs to draw the interspace together and the muscle closed tight with full expansion of the lung during the final closure. It may be wise to spray crystalline penicillin and streptomycin in the chest cavity and wound before final closure.

*Postoperative care* must be meticulous. The neurological state should be assessed as early as possible. Pulmonary atelectasis must be vigorously prevented by coughing, deep breathing, etc. The underwater drain can be removed when it becomes walled off and so ceases to fluctuate (usually in 48 hours). A postoperative chest film in 24 hours is useful to rule out hæmothorax or pneumothorax.

#### SUMMARY

The term "cardiac arrest" includes cardiac standstill and ventricular fibrillation.

Thirty-four cases of cardiac arrest in heart surgery are analyzed.

The intimate steps in the management of cardiac arrest are described.

Electrical defibrillation is usually essential in the treatment of ventricular fibrillation.

The authors feel that the important underlying factor in most cases of cardiac arrest is hypoxia. The essential danger lies in the inability of the anaesthetist and surgeon to recognize these minor but significant degrees of oxygen lack during surgery.

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### RÉSUMÉ

L'hypoxémie constitue souvent un facteur important d'arrêt cardiaque, qu'il est quasi impossible d'évaluer uniquement par des moyens cliniques. L'emploi des curarisants peut aggraver ce risque en gênant le mécanisme de la respiration. L'évacuation soudaine d'une accumulation de CO<sub>2</sub> par l'instauration d'un contrôle vigoureux de la respiration de la part de l'anesthésiste peut provoquer un arrêt cardiaque. L'hypotension, qu'elle soit due à une manipulation excessive des viscères ou à l'hémorragie, présente les mêmes dangers.

Le cerveau et le cœur sont également sensibles à l'hypoxémie et ne peuvent la subir pour plus de 4 minutes sans en ressentir des effets graves et permanents. Le cœur d'un sujet jeune et sain peut la tolérer mieux et plus longtemps que celui d'un sujet âgé et qui aurait pu, par ailleurs, en souffrir d'une manière intermittente et transitoire antérieurement.

Les 34 cas sur lesquels est basé ce travail comprenaient 26 cas de fibrillation ventriculaire, dont plusieurs furent traités avec succès par la défibrillation électrique. La presque totalité de cette série provient de chirurgie

cardiaque. Les auteurs tiennent à faire la distinction entre un cœur normal s'arrêtant subitement sous l'effet d'influences néfastes et un cœur malade, épuisé et rendu à bout de ses ressources; ils suggèrent le terme "arrêt cardiaque" comme étant justifié dans le premier cas, et "incompétence cardiaque" pour le second.

Environ un cas sur six d'arrêt cardiaque se produit hors de la salle d'opération (salle des plâtres, de cystoscopie, etc.). Des trousses pour intervention cardiaque d'urgence devraient être disposées dans des endroits stratégiques de l'hôpital afin de pouvoir servir à un instant d'avis. Les signes cardinaux d'arrêt cardiaque sont l'absence de pulsation artérielle et l'abaissement de la tension à zéro. La technique de l'intervention est basée d'abord sur l'installation de la respiration contrôlée, habituellement par l'entremise d'intubation endotrachéenne, et ensuite par la manipulation directe du myocarde après incision de la paroi thoracique, de la plèvre et du péricarde. Au cours d'opérations sur l'abdomen, le cœur peut être massé au travers du diaphragme sans qu'il soit nécessaire d'entamer celui-ci. Les détails de chaque méthode sont donnés dans le texte. Le tonus myocarde est d'importance primordiale dans la reprise des battements; il peut être conservé grâce à l'injection intracardiaque de médicaments tels que le chlorure de calcium ou l'adrénaline (1:10000). La posologie exacte de ces adjuvants n'a pas encore été définitivement établie. Si le rythme normal tarde à reprendre, l'aorte peut être mobilisée partiellement juste en aval de la sous-clavière gauche, et comprimée avec une pince Kelly longue, en vue de réduire le champ vasculaire et d'améliorer la circulation dans les coronaires.

Le massage cardiaque doit être continué jusqu'à la reprise des battements spontanés ou jusqu'à l'apparition des signes irréversibles de la mort réelle. (On a déjà rapporté des ressuscitations après 8 heures de massage.) L'application de courant électrique en fibrillation ventriculaire doit être précédée de massage cardiaque afin de restaurer le tonus du myocarde. La manipulation peut quelquefois suffire par elle-même. L'article se termine sur les précautions qu'il faut observer dans la période post-opératoire dans les cas où un arrêt cardiaque a été combattu par les techniques décrites ci-haut.

M.R.D.

### A CLINICAL STUDY OF "FRENQUEL" (ALPHA (4-PIPERIDYL) BENZHYDROL HYDROCHLORIDE) IN CHRONIC SCHIZOPHRENIA\*

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PIPRADOL, OR alpha - (2 - piperidyl) - benzhydrol hydrochloride (Meratran), is a non-specific stimulant to activity which exacerbates the visible effect of hallucinations in psychotics.<sup>1</sup> In animal experiments it has been shown to

affect the central reticular substance<sup>2</sup> and the septal area.<sup>3</sup>

Alpha - (4-piperidyl) - benzhydrol hydrochloride, the gamma-isomer of pipradol ("Frenquel"), which was subsequently developed, has been shown to have certain properties opposite to those of pipradol in the experimental animal, namely a mildly depressant action and the ability to prolong barbiturate sleep and to neutralize the hyperacidity caused by pipradol. It has been shown to have a low toxicity, although large continued doses produce fatty infiltration of the liver in rats.<sup>4</sup>

Clinically it has been found to exert a blocking effect against LSD-25 (lysergic acid diethylamide) psychosis, preventing the development of hallucinatory activity when used as a premedication or terminating it rapidly when given intravenously. It has also been found

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effective in blocking mescaline psychosis.<sup>5</sup> In the rabbit it rapidly counteracts electroencephalographic (E.E.G.) changes produced by LSD-25 or mescaline when given proportionately to the amount of hallucinogen administered.<sup>6</sup> In the human experiments it does not block the visceral effects of LSD-25. In the animal experiments the mydriasis produced by LSD-25 or mescaline remains unaltered, suggesting that its blocking action is limited to the central nervous system.<sup>6</sup>

Therapeutically it has been used in various psychiatric conditions. In a double-blind study of 39 long-stay patients (38 of whom were chronic schizophrenics), treated for four weeks with oral doses of 20 mg. Frenquel daily, 21 were stated to show definite improvements and 7 doubtful improvements in the features selected for study. Improvement consisted mainly in reduction of overactivity, in better ward adjustment, and to a lesser extent in more appropriate thought and behaviour and reduction of hostile feelings.<sup>7</sup>

Working with a much larger case material and over a longer period, Fabing<sup>8</sup> used Frenquel in oral doses of up to 400 mg. daily. Of 14 acute schizophrenics, ill less than five months, five appeared to recover in one to three days; three others improved and recovered after electroconvulsive therapy or chlorpromazine was added. Of 34 chronic schizophrenics 8 made a full adjustment with Frenquel alone, and 8 others with Frenquel plus chlorpromazine and/or electroshock. The author also found Frenquel to be probably of value in alcoholic psychoses, senile dissociation reactions and postoperative confusional states.

More recently Proctor and Odland<sup>14</sup> reported that Frenquel improved 5 out of 17 chronic psychotics, the unimproved cases all having some form of organic cerebral deterioration; that it markedly improved 20 and moderately improved 6 out of 34 acute psychotics, 12 of the markedly improved cases being schizophrenics, and those with no improvement being mostly organic cases; and that it completely alleviated symptoms within a matter of hours in all but 3 of 19 cases of acute alcoholic hallucinosis.

#### THE INVESTIGATION

In view of the evidence that Frenquel was a blocking agent in certain model psychoses, and the hypothesis that it might have an opposite

action to pipradol, which in our experience increased the intensity or effect on conduct of existing hallucinations,<sup>1</sup> we set up a pilot study of its clinical effects.

Eighteen patients were selected, the main criterion being the presence of disturbing and more or less constant hallucinations. The length of hospitalization varied from three months to 39 years: 5 patients had been in hospital one year or less, 6 patients one to ten years and 7 over ten years. The diagnostic categories were: paranoid schizophrenia 11; catatonic schizophrenia 3; schizophrenia, other types 3; alcoholism with psychosis 1.

A double-blind study was not set up, as the experiment was of a pilot nature, and we wished to learn more about the drug's therapeutic possibilities before undertaking a more exact study. However, all the cases were kept in the same environment as beforehand, and all were well known to the observers and ward staff. No measures other than Frenquel administration were used during the observation period—no electroshock, no other drugs, no "total push" program.

The patients were treated for an average of 49 days (shortest 17 days; longest 81 days) with up to 400 mg. Frenquel daily by mouth. All were vividly and actively hallucinated, and showed this in their behaviour.

A daily chart was kept by the nursing staff on each patient, showing particularly any changes in activity, especially stereotyped activity and hallucinations, for these were the features which had increased with pipradol.

Each patient also had complete blood counts, urinalysis, non-protein nitrogen (N.P.N.) estimations and thymol turbidity tests before, during and after the course and was weighed weekly.

Daily observation was given by the ward-staff physician, and psychiatric examination before and during the course by one of the authors.

#### RESULTS

*Psychiatric:* These were completely negative. No side-effects were seen from the drug, and no dramatic changes. The ward and psychiatric staff were unanimous in classifying only one case as "slightly improved" and the remainder "unchanged".

**Physical:** No significant changes in appetite or weight were recorded for any of the patients receiving Frenquel. There were no dramatic changes in the blood count, urinalysis or thymol turbidity test. The N.P.N. estimations, however, in 11 cases showed a consistent and statistically significant rise toward the upper limit of normal. The average pre-treatment level was 32 mg. %; the average after one month on treatment (18 cases) was 40 mg. %; the average after two months on treatment (10 cases) was 43.4 mg. %. The average one month after treatment (6 cases) was 46 mg. % and the average two months after treatment (5 cases) was 40 mg. %. Individual case levels are shown in Table I.

to colour the picture. Osmond and Smythies<sup>12</sup> point out that the phenomena produced by the drug (in this case mescaline) should not be compared with that of the group of schizophrenias *en bloc*, but that, logically, acute mescaline symptomatology should be compared with that of acute schizophrenia, and chronic mescaline symptomatology with that of chronic schizophrenia. Since mescaline is not a drug of addiction, chronic poisoning is virtually unknown, and consequently this comparison of "chronic" states cannot be made.

Hoch<sup>9</sup> states that under mescaline a complete schizophrenic dissociation is much more prominent in schizophrenics and latent schizophrenics than in "normals". In the latter the symptoms

TABLE I.—RELATION OF N.P.N. READINGS TO DOSES OF FRENQUEL AND LENGTH OF TIME ON TREATMENT  
FIVE SELECTED CASES

Case No.	Pre-treat.	N.P.N. Readings			
		After 30 days dose 200 mg.	After 60 days dose 400 mg.	30 days post-treat.	60 days post-treat.
1.....	17.5 mg. %	33.16 mg. %	46.0 mg. %	38.0 mg. %	40.8 mg. %
3.....	31.5 mg. %	42.4 mg. %	49.2 mg. %	50.0 mg. %	47.6 mg. %
4.....	24.5 mg. %	33.0 mg. %	44.4 mg. %	50.8 mg. %	30.8 mg. %
5.....	31.5 mg. %	37.24 mg. %	46.4 mg. %	47.6 mg. %	42.6 mg. %
7.....	18.9 mg. %	34.8 mg. %	48.0 mg. %	48.4 mg. %	37.4 mg. %

The number of cases reported in the table is too small to permit any major conclusion to be drawn. Attention is drawn to our findings, however, as indicating a need for estimating the N.P.N. in future studies on the drug.

#### DISCUSSION

The phenomena of mescaline and LSD psychoses are essentially similar,<sup>15, 16</sup> and since Frenquel is reported to block both forms of psychosis,<sup>5</sup> both will be considered here in relation to schizophrenia.

Opinions vary as to the nature of the phenomena in these drug psychoses. In general, European authors stress the organic nature of them and American authors the schizophrenic. While some cases of acute schizophrenia are clinically indistinguishable from the drug psychoses, and notwithstanding the schizoid symptomatology described in the latter by many authors, the analogy between drug psychoses and schizophrenia can be overstressed, certainly so far as conclusions as to therapy are concerned. In neither condition is it known which phenomena are really primary and which secondary, and in both the personality enters in,

are more organic combined with some schizophrenic. He considers that the *differences* between LSD and mescaline psychoses in normals and schizophrenia itself, do not permit an analogy to be drawn between the two conditions.<sup>13</sup> Mayer-Gross<sup>10</sup> considers that, although symptoms of mescaline and schizophrenia have been compared, it is much more "the strangeness experienced by the patient suffering from schizophrenia and the difficulties of describing what is happening in the two conditions which are similar".

Stockings<sup>11</sup> thinks that, although many features of mescaline psychosis resemble schizophrenia, the type and quality of the visual experiences relate it more closely to the toxic-confusional psychoses, while the mood changes resemble an affective reaction. It is not identical in form with any naturally occurring psychosis.

Rorschach testing, also, does not give an unequivocal picture. Some authors emphasize the schizophrenic and paranoid distortions under LSD: the autistic thinking, the decreased organization, the contamination responses, the lack of logical thinking, the negativism and the diminished emotional inhibition. They also point



out the similarity of tests of concrete-abstract thinking to those in schizophrenics.<sup>19</sup> The difficulty again is to know whether these regressive and primitive phenomena tapped by the test are primary disturbances in schizophrenia.

On the other side of the picture, Delay and his co-workers<sup>17</sup> quote their own experiments and Stoll's work on the Rorschach in LSD psychoses to show that all the personality traits in the normal protocol, especially the introverted elements, are increased by LSD and that a toxic syndrome is added to the picture. Stoll concluded that the combination of organic and schizophrenic signs was absolutely typical for the drug psychosis and that the same non-specific picture could be found under alcohol and mescaline. Other authors have also found Rorschach data to show a connection between subjective responses after drugs and the personality state of the subject.<sup>18</sup>

In general, therefore, the position as regards mescaline and LSD psychoses may be summarized as follows: they show phenomena of the organic reaction which in most cases do not dominate the picture, combined with symptoms similar to those occurring in schizophrenics, the whole being influenced by the subject's own personality. The clinical resemblance is closest to the acute schizophrenias and to the acute toxic hallucinosis.

Suggestive facts are offered by comparison of the effects of the drugs in existing psychiatric conditions. When mescaline was given to chronic schizophrenics, the patients were able to distinguish the drug phenomena from their own endopsychic experiences. On the other hand, patients in delirium showed an increase of delirious symptoms and made no comment on the new material.<sup>20</sup> This would relate the drug psychosis to toxic states and acute states generally.

Probably one of our major difficulties in making comparisons lies in the circumstance that we are by no means clear as to the nature of an acute schizophrenia. We may be dealing with a reaction-type of an acute kind in response to an unknown factor, the picture varying from case to case in accordance with the patient's unconscious and particular temperament; or we may be dealing with several types of disease process, each of which shows features we call schizophrenic by the involvement of a common mechanism. If we accept the latter hypothesis

and assume that LSD and mescaline psychoses also involve this common mechanism, we may justifiably try the effects of agents which experimentally block the drug psychoses in the natural variety.

Various agents are reported to affect both natural and experimental psychoses. Sodium Amytal can abolish the affective reaction of mescaline.<sup>9</sup> Nicotinic acid is reported to reduce all the disturbances of LSD except the affective.<sup>25</sup> The ubiquitous twins, reserpine and chlorpromazine, can produce a noticeable attenuation of LSD symptoms when used prophylactically or therapeutically.<sup>21</sup> Intramuscular chlorpromazine has effectively interrupted LSD psychosis at its peak, though with minimal effect on the electroencephalogram.<sup>22</sup> In mescaline psychosis chlorpromazine has been shown to diminish tension and anxiety, and reverse the E.E.G. changes and mydriasis, as well as the mental symptoms.<sup>23</sup>

Such agents as chlorpromazine probably block the drug psychosis indirectly by, on Fischer's thesis,<sup>24</sup> preventing mediation of the stress response.

The anxiety and tension felt by the subject in a drug psychosis, as the result of his distorted perception and consequent inability to keep his grip on reality, may as Hoch<sup>9</sup> suggested be the factor leading to the depressive and paranoid reactions. Sodium Amytal, reserpine and chlorpromazine reduce tension and so may indirectly block a drug psychosis. In the case of chlorpromazine the objective autonomic effects are also antagonized. Frenquel, on the other hand, does not affect the autonomic system and had no tranquillizing effect on our patients. We cannot confirm that Frenquel has any value therapeutically in chronic schizophrenia, either on the total state or on the hallucinations as a symptom—and our dosage was considerably higher than that of other authors. The dramatic results reported by Proctor and Odland<sup>14</sup> in cases of delirium tremens certainly warrant further trial of Frenquel in this condition, and if confirmed would point to a common mechanism in it and LSD and mescaline psychoses. The position regarding acute schizophrenia is less clear. Diagnosis of this condition is often difficult or controversial and cases recovering rapidly without therapy would probably be given a different diagnostic label in retrospect: an affective psychosis, a

symptomatic psychosis, or a delirious state. Diagnosis is all the more difficult when one or other of these reactions occurs in a schizoid individual, and may indeed only be possible in retrospect. Until some exact test of schizophrenia is available our estimate of therapy in acute schizophrenia must be weighted by this fact.

# SUMMARY

Alpha - (4-piperidyl) - benzhydrol hydrochloride (Frenquel), reported to be a blocking agent in lysergic acid diethylamide and mescaline psychoses, was given to 18 chronic schizophrenics, all of whom were vividly and constantly hallucinated. Dosage varied up to 400 mg. orally daily for an average length of treatment of 49 days.

No changes of any significant kind were seen in any of the patients.

The use of the drug, as reported by other authors, is briefly discussed.

The clinical relationship between model and endogenous psychoses is discussed.

Our thanks are due to W. Schlichter, M.D., of this hospital for his clinical observations, to the ward staff concerned in the investigation, to Stuart Schultz, M.D., Medical Superintendent, for his encouragement, and to the William S. Merrell Co., Cincinnati, Ohio, for their generous supply of Frenquel.

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# RÉSUMÉ

Si le pipradol (Meratran, marque déposée) a la faculté d'accentuer les hallucinations des psychosés, son isomère gamma (Frenquel, marque déposée) par contre a une action contraire et peut même prolonger le sommeil que produisent les barbituriques. Il s'oppose à l'action du diéthylamide de l'acide lysergique (L.S.D. 25) et de la mescaline. Vingt-et-un malades d'une série de 39 auraient accusé une amélioration après 4 semaines de traitement, manifestée surtout par une diminution de l'agitation, de l'hostilité et une meilleure adaptation au milieu hospitalier. Certains auteurs s'en servaient comme adjuvants des électrochocs ou de la chlorpromazine.

Le présent article fait part des résultats obtenus à l'Hôpital des maladies mentales de Brandon, Manitoba, dans le traitement au Frenquel de 18 aliénés parmi lesquels se trouvaient des schizophrènes simples, paranoïaques et catatoniques et un alcoolique. Les doses atteignent 400 mg. par jour. Aucun changement psychiatrique, physique ou biochimique ne fut observé sauf une élévation progressive du taux de l'azote non protéinique du sang, pendant la durée du traitement.

On est porté à croire que les psychoses causées par la mescaline et L.S.D. 25 présentent le caractère de certaines réactions organiques sans que celui-ci domine le tableau; on y trouve en plus des symptômes propres aux schizophrènes, et le tout est influencé par la personnalité même du sujet.

M.R.D.

# NEW DRUG FOR TENSION AND ANXIETY

Yet another compound for the symptomatic treatment of tension and anxiety is reported in the October issue of *Antibiotic Medicine and Clinical Therapy* (3: 329, 1956). Ferguson and Linn report studies of 2-ethylcrotonylurea (Nostyn) in the treatment of 142 psychotic women. Animal experiments had indicated that the compound was of very low toxicity and had a wide sedative range. The drug does not depress blood pressure or respiration, has no analgesic or anticonvulsive properties, and is readily absorbed on oral ingestion. Most of the patients in the present study had schizophrenia. They were selected on behaviour pattern rather than diagnosis, and were treated with 2-ethylcrotonylurea for periods up to eight months, the daily dose varying from 150 to 1800 mg. No signs of toxicity were discovered and no need was found to administer more than 900 mg. daily. Moderate overactivity was controlled, but severe overactivity was less controlled than with reserpine. In 82% of anxious and tense patients the drug produced sedation, without hypnosis or hang-over. The drug was more effective than meprobamate and could be used to replace reserpine and barbiturates as a sedative.



## PHYSIOLOGICAL AVAILABILITY OF DRUGS IN TABLETS\*

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THE CLINICAL EFFECTIVENESS of tablets and capsules depends on at least two factors. The drug must be present in the labelled amount and it must be available to the patient. While it is relatively simple to assay a preparation and ensure that it meets labelled claim, it is more difficult to determine whether it is available to the patient. Actual demonstration of clinical effectiveness, while of prime importance, is not amenable to routine testing procedures. In an attempt to ensure availability of medicaments in tablets, various disintegration methods and times are specified in pharmacopœias. With the exception of work<sup>1</sup> from this laboratory, however, few attempts have been made by the pharmaceutical industry or by regulatory bodies to relate such tests to quantitative measures of the physiological availability of the ingredients of tablets. The situation at the present time does not appear to have changed, except perhaps for the introduction by certain pharmaceutical manufacturers of more "timed" disintegrating or delayed-action medication. As far as can be ascertained, there is little published information based on quantitative physiological studies to support the claims which are being made for these "timed" disintegrating products. In view of this situation, it is the purpose of this paper to discuss the importance of determining the physiological availability of drugs and of using such data as the basis for any disintegration tests.

### BASIS OF DISINTEGRATION TESTS

While it is most desirable that disintegration tests reflect the availability of a drug to the patient, neither the British Pharmacopœia,<sup>2</sup> nor the U.S. Pharmacopœia,<sup>3</sup> nor the National Formulary,<sup>4</sup> has tests which have been evaluated on this basis. Indeed, the statement contained in the U.S.P. XIV<sup>5</sup> that "a coating may be applied to official tablets and capsules, provided that it will disintegrate in the alimentary tract" has been modified in the U.S.P. XV<sup>3</sup> by the deletion of

any reference to disintegration in the alimentary tract. At least one group, however, the War Food Administration in the United States,<sup>6</sup> has recognized the importance of physiological availability by requiring that vitamins in products purchased by them be present not only in sufficient total quantities but also in a form completely available to the human when the product is swallowed whole.

While a great number of *in vitro* disintegration tests are reported in the literature, there appears to be very little information available on their actual physiological validity as judged by excretion studies. This situation has occurred in spite of the fact that Oser and his associates<sup>6</sup> have reported that urinary excretion is the only true measure of physiological availability of the water-soluble vitamins. Kanig,<sup>7</sup> in discussing enteric coatings, has stated: "It is obvious that it is difficult, if not impossible, for human subjects to be utilized in a repeated quality control procedure of testing during large-scale production. For this reason it is of added importance that an established and standardized *in vitro* testing method be utilized as an additional check in the manufacturing laboratory." Filleborn<sup>8</sup> has pointed out that simple *in vitro* disintegration tests are of value only if shown to agree with *in vivo* disintegration times. Kline<sup>9</sup> has explained further that urinary excretion tests require rather close control of the diets of the test subjects. For this reason they are cumbersome to use as routine procedures. They are also costly and time-consuming. The need for the simplification of these tests or the development of *in vitro* procedures which have been correlated with them is obvious. Thus, while some authorities have defined the problem, little progress seems to have been made in solving it.

### WORK OF FOOD AND DRUG LABORATORIES

In 1953, studies were initiated in the Food and Drug Laboratories to develop an *in vitro* method for the determination of the disintegration time of coated tablets and to relate this time to the physiological availability of the medicaments, using a urinary excretion technique. The disintegration apparatus was that described in the U.S.P. XIV<sup>5</sup> with the addition of slight rubbing action provided by either a rubber or plastic disc. Simulated gastric or intestinal juices were used as the disintegration media.

In the first project, Chapman, Crisafio and Campbell<sup>1</sup> studied the relationship between the *in vitro* disintegration time of sugar-coated tablets and the physiological availability of riboflavin. Most of these tablets were simple coated tablets but at least one was an enteric-coated tablet. In all, 25 tablets were examined both from the standpoint of disintegration time and physiological availability. It was found that those

\*From the Food and Drug Laboratories, Department of National Health and Welfare, Ottawa.

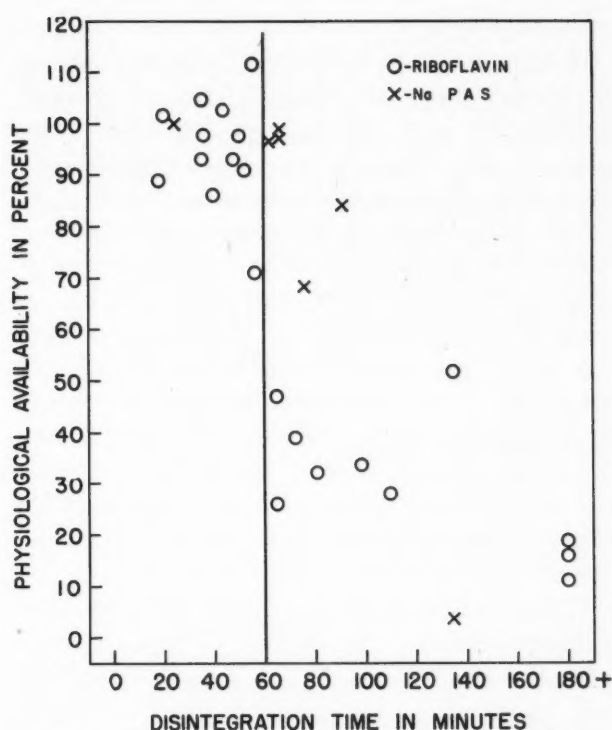


Fig. 1.—Relationship between physiological availability and disintegration time.

tablets having disintegration times exceeding one hour (30 minutes in simulated gastric juice and 30 minutes in simulated intestinal juice) were not completely available.

This study was criticized<sup>9</sup> on the basis that some tablets might release their riboflavin content to the body at such a rate that it would be utilized as quickly as it was released and hence would not be excreted in the urine, and that therefore low excretion of riboflavin would not necessarily indicate low availability of riboflavin from that tablet. This possibility was investigated, and it was found<sup>10</sup> that for 1, 3 and 5 mg. quantities of riboflavin the excretion was the same whether these amounts were taken as a single dose or in 10 small doses totalling the same amount.

While the studies to relate *in vitro* disintegration time with physiological availability using riboflavin as the marker appeared to be quite conclusive and satisfactory, there still remained the possibility that some other drug might give a different picture of availability. A non-metabolite might react differently from riboflavin, which is metabolized to a large extent. Accordingly, Chapman, Crisafio and Campbell<sup>11</sup> repeated the comparison of disintegration time and physiological availability on a smaller scale, using sodium *p*-aminosalicylate as the marker. They showed that sodium *p*-aminosalicylate tablets having disintegration times longer than 67 minutes were not completely available.

The results of the two studies carried out in the Food and Drug Laboratories to relate *in vitro* disintegration time with physiological availability are summarized in Fig. 1. The line drawn at the 60 minute disintegration time indicates the limit considered permissible based on the data obtained. For those tablets having disintegration times lying between 60 and 70 minutes there is some doubt regarding the quantitative availability of their medicaments. There is no doubt of the low availability of riboflavin in this area but it is evident that more data on *p*-aminosalicylate or related compounds may be desirable. While some sodium *p*-aminosalicylate tablets having disintegration times of 67 minutes were almost 100% available, two riboflavin tablets having disintegration times of 64 minutes had availabilities of 47% and 26%. It may be noted that riboflavin data<sup>1</sup>

on three tablets, which had disintegration times of 75-95 minutes and which were quantitatively available, were omitted from Fig. 1. It was found that the riboflavin had been placed in the outer layers of these tablets and was dissolved out before the core of the tablet had disintegrated. Obviously, these tablets were not satisfactory for such a study, because any indicator must be in the core of the tablet.

As a result of the work described above, a clause has been incorporated into the Food and Drug Regulations which requires that all tablets, except enteric-coated or timed-disintegrating, should disintegrate in not more than 60 minutes when tested by the Official Method of the Food and Drug Laboratories.

#### TIMED-DISINTEGRATING TABLETS

A recent survey carried out by these Laboratories indicates that there are at least 60 products, sold by 22 manufacturers, available on the Canadian market which are claimed to be timed-disintegrating. These products fall into the following categories: (1) capsules containing small pellets which have varying disintegration times, (2) tablets with part of the medicament in the outer layers and part in the core, (3) tablets with an enteric coating, (4) compressed tablets in which are embedded particles having varying disintegration times and (5) compressed tablets made up of three layers having varying disintegration times. Eleven different brands of tablets (types 2 and 5 above) claimed to be timed-disintegrating have been examined from the standpoint of *in vitro* disintegration time. As is shown in Table I, only one brand of these tablets has an *in vitro* disintegration time of less than 60 minutes. If this limit can be applied to the substances in these tablets, it would mean

TABLE I.—DISINTEGRATION TIMES AND CLAIMS MADE FOR TIMED-DISINTEGRATING TABLETS

Product	In Vitro Disintegration Time		Claims made for release of Medicaments
	As found by Food and Drug Laboratories In minutes	As reported by Manufacturer in minutes	
A	57	150	One half for early action
B	67	—	One half for delayed action
C	85	180-360	Timed disintegrating tablets
D	92	240-300	Part for immediate release and part for repeat dose
E	98	180-360	One half for immediate release and one half for delayed action
F	111	180-300	One half for immediate release and one half for delayed action
G	157	240-300	Part immediately available and part 2-3 hours later
H	193	—	One half for immediate release and ½ for delayed action
I	210+	480-600	Action delayed until 4-6 hours after ingestion
J	300+	180-360	Constructed to release components over an 8-10 hour period
K	330+	480-600	Medicaments in outer coating and in enteric core
L	420+	390	Constructed to release the active components over an 8 to 10 hour period
			Prolonged action



that ingredients in 10 of the brands may not be fully available to the consumer. Furthermore, there appears to be a great discrepancy between the disintegration times reported by the manufacturers and those found by the Food and Drug method. In most cases the manufacturer used the U.S.P. XV method. The only major difference in the procedures used was the insertion of a plastic disc to provide rubbing action in the Food and Drug Laboratories method. This has been shown to improve the precision of the method and to shorten slightly the disintegration times of some tablets.

TABLE II.—DISINTEGRATION TIMES OF AND CLAIMS MADE FOR OTHER  
"TIMED-DISINTEGRATION" CAPSULES AND TABLETS

Company No.	Type of Product	No. of Products	Claims	In Vitro disintegration times supplied by company (hours)
1 .....	Tablet containing embedded pellets	3	Sustained over 10-12 hours	Several 11-13
2 .....	"	2	Slow release, prolonged therapy for 10-12 hours	
3 .....	Capsules containing pellets	3	Part for immediate release, part in 3-4 hours and part in 8 hours	4-5
4 .....	"	1	Timed disintegration throughout 6-10 hours	6
5 .....	"	6	Sustained release capsule	4-8
6 .....	"	2	Sustained release form	—
7 .....	"	1	Released gradually over approximately 8 hours	—
8 .....	"	1	Part for immediate release, part in 4 hours and part in 8 hours	—
9 .....	"	2	10-12 hours' release	—
10 .....	"	3	Timed disintegration throughout a period of 6-10 hours	—
11 .....	"	2	Disintegrates during a period of 6-10 hours	—
12 .....	"	3	Timed disintegrating medication	—
13 .....	"	3	Prolonged disintegration for 8-10 hours	—
14 .....	"	1	Slow disintegration, controlled absorption	—

Other timed-disintegrating preparations are listed in Table II. It may be noted that these are either tablets or capsules containing pellets of varying disintegration times. These serve to illustrate the number and type of preparation available on the Canadian market. It is claimed that most of these preparations release their medication over an 8 to 12 hour period. No published means of testing the *in vitro* disintegration of these preparations is at present available although studies have been initiated.

## DISCUSSION

All of the tablets used in the studies carried out in the Food and Drug Laboratories were sugar-coated and only one was claimed to be enteric-coated. There was evidence that some of the tablets had coats which were resistant to gastric juice. It has been argued that enteric-coated tablets should not be considered along with other tablets. From the point of view of availability, however, there seems no logical reason for enteric-coated tablets to be considered differently from other tablets. The important point appears to be that tablets having disintegration times greater than 60 minutes cannot be relied upon to be quantitatively available, whether they are considered to be enteric or simple coated tablets.

There seem to be rather wide differences of opinion regarding tablet disintegration times. Published results relating *in vitro* disintegration time to physiological availability do not seem to have been widely accepted in spite of the fact that no better criteria are available. There has also been some question regarding the rate and site of absorption of drugs. While it is possible that other medication may not be absorbed in the same way as riboflavin or sodium *p*-aminosalicylate, there appear to be few data to substantiate this view. Vliet<sup>12</sup> has stated recently, in reference to the work of Chapman, Crisafio and Campbell, that some of the tablets used may have been enteric-coated and would not become available until they reached the intestinal tract. He has stated further that, on the other hand, a simple coated tablet would start to disintegrate earlier and that this tablet might show a high degree of total drug availability even though it required two hours or more for complete disintegration. No data, however, were presented to support this view.

With regard to the timed-disintegrating tablets, very specific claims are being made for the rate at which they disintegrate in the body. However, an editorial appearing in the *New England Journal of Medicine*<sup>13</sup> states that "there could be a great difference between disintegration and absorption times, depending on what part of the intestine the drug had reached". With the exception of one or two companies, these claims are based either on data which have been obtained by *in vitro* methods or on qualitative expressions of clinical effectiveness. Discussions with representatives of some manu-

facturers indicate that it is their feeling that *in vitro* times are directly equivalent to *in vivo* disintegration times. Such observations are not in agreement with existing data on physiological availability, which indicate that *in vitro* disintegration times are probably a fraction of the *in vivo* times. It must be concluded that either the rate of absorption of many of these drugs is much different from riboflavin and sodium-*p*-aminosalicylate, or that large proportion of the drug dose in these tablets is unavailable.

While results reported in several papers<sup>14-17</sup> would suggest that timed-disintegrating products exert a prolonged clinical response, none of these report the quantitative physiological availability of the medicaments. Some manufacturers have demonstrated that their preparations are clinically effective. Thus patients apparently are receiving sufficient dose of the drug to obtain the relief desired. The remainder of the dose, however, which could be a significant proportion, may not necessarily be absorbed. Clinical effectiveness is therefore not necessarily an indication of complete physiological availability. On the other hand, physiological availability ensures that the drug is absorbed and therefore, if sufficient dose is taken, it must be clinically effective. It has been suggested that in the case of certain timed-disintegrating tablets, in order to gain the advantage of clinical therapy over a longer period of time, it may be difficult to achieve complete physiological availability. Since clinical responses are not amenable for use as routine testing procedures, physiological availability studies appear to offer a convenient means of ensuring clinical response. In those cases where delayed-action medication is not fully available physiologically, it is most important that *in vitro* procedures be standardized very carefully against some quantitative measure of clinical response. More work needs to be done to determine whether, in fact, a delayed-action preparation which gives the desired clinical response can be made fully available.

Occasionally x-ray data have been used to indicate disintegration within the intestine. Feinblatt and Ferguson<sup>18</sup> have conducted an *in vivo* roentgenographic study of timed-disintegration capsules to compare *in vivo* and *in vitro* times and have reported that the disintegration times using their technique are similar to but longer than the times found using the U.S.P. *in vitro* method. However, Oser *et al.*<sup>6</sup> have pointed out

that x-ray information is also subject to criticism.

The possibility has been advanced by some manufacturers that the rate of absorption and excretion of certain drugs may be quite different from that of others. In this connection, it is interesting to review briefly a few pertinent observations. Melnick *et al.*<sup>19</sup> have shown that the absorption excretion patterns over a 24-hour period for thiamine, ascorbic acid and niacinamide are similar to that of riboflavin. Best *et al.*<sup>20</sup> have recently shown that an oral dose of vitamin B<sub>12</sub> is largely excreted within the next 24 hours. The rate of excretion of *p*-aminosalicylate has been shown to be similar to that of riboflavin. It is influenced in a similar manner by slow disintegration.

#### SUMMARY

(1) To ensure complete availability, simple tablets should have an *in vitro* disintegration time of less than 60 minutes as determined by the official method. (2) There is little, if any, evidence at present to suggest that this time should not apply to all types of tablets regardless of whether they are compressed, simple coated, delayed action or enteric coated tablets. (3) Physiological availability appears to be the most satisfactory basis for any *in vitro* disintegration test. (4) Claims made for timed-disintegration products must be supported by critical *in vitro* and *in vivo* tests.

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## RÉSUMÉ

Il n'existe aucune épreuve permettant de vérifier la durée de désintégration d'un médicament dans le système gastro-intestinal et, de là, son absorption dans l'organisme. Les auteurs s'accordent pour affirmer que les épreuves *in vitro* sont loin de correspondre dans bien des cas aux processus physiologiques, et que le meilleur moyen d'établir le taux d'absorption chez un sujet est de mesurer l'excrétion urinaire. Certaines épreuves pratiquées sur des comprimés de riboflavine enrobés de sucre, grâce à un appareil reproduisant les mouvements péristaltiques par l'entremise de disques de caoutchouc, montrèrent que les pilules dont la désintégration prenait plus d'une heure étaient incomplètement absorbées. (Elles étaient exposées à une solution de suc gastrique pendant 30 minutes et à une autre solution de sécrétions intestinales pendant 30 autres

minutes.) Les mêmes tests répétés sur du para-amino-salicylate de sodium donnèrent des résultats semblables. Il existe une grande quantité de médicaments dont la présentation est censée assurer une désintégration à retardement. Après vérification, il appert que les temps de désintégration des fabricants ne correspondent pas à ceux que les auteurs de ce présent article ont trouvés; de plus, il se peut que la majorité de ces produits ne soit qu'imparfaitement absorbée. En dépit des objections que formulent les fabricants à l'égard de la méthode d'évaluation précitée, les auteurs ne voient aucune raison de ne pas appliquer intégralement leurs conclusions aux comprimés enrobés comme à ceux qui ne le sont pas. A mesure que les données s'accumulent, il semblerait qu'un nombre de médicaments sont absorbés et excrétés d'une façon semblable à celle de la riboflavine et du para-amino-salicylate. M.R.D.

## AGING AND OSTEOARTHRITIS

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DESPITE THE EXTENSIVE LITERATURE on osteoarthritis our present knowledge of this disease is still unsatisfactory. All writers on osteoarthritis agree that pain is the most characteristic symptom in this disease. It is common knowledge, however, that pain may be an unreliable symptom in some cases. Clinical signs of osteoarthritis are very scanty. Such signs as stiffness and rigidity are typical of osteoarthritis if they are present, but there are many cases of this disease in which all objective clinical evidence is completely lacking. The situation regarding pathological signs is only a little better. In osteoarthritis, the bones, synovial membranes, and cartilages present a typical macrostructure and microstructure, but these can of course be seen only after death. In living man, only radiography may enable us to detect initial or advanced signs of osteoarthritis and to follow the progress of the disease over a period of time. The following radiographic signs are generally recognized as typical of osteoarthritis: exostoses, lipping in various stages of development, calcification of joint cartilages, ligaments, joint capsules or soft tissues in the vicinity of the joint, narrowing or disappearance of the radiological joint and the intervertebral spaces due to degeneration of cartilage, and osteoporosis of various grades. At first sight, it would

seem that the diagnostic problem of osteoarthritis is very easy to solve in the presence of so many radiographic signs, but this simplicity is only apparent. Only recently, Lowman<sup>18</sup> has written the following:

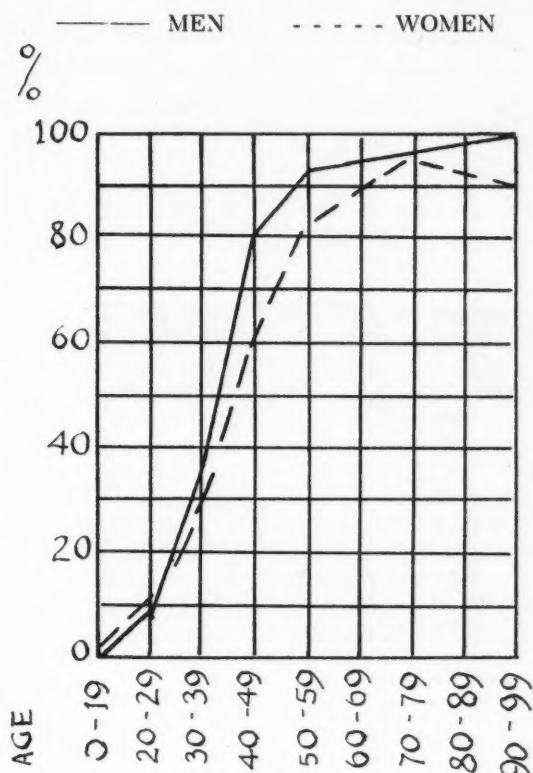
"Roentgenographs (of osteoarthritis) are of value as confirmatory evidence of clinical symptoms. Since 95% of persons with evidence of degenerative joint disease are asymptomatic, the demonstration of changes roentgenologically is of no significance *per se*. Furthermore, the extent of damage demonstrable by x-ray examination is no measure of joint incapacity since major changes may be dissociated with minimal clinical symptoms and vice versa. Total clinical evaluation is the only valid yardstick for management of the individual patient. In other words: roentgenographic signs (i.e. morphological evidence) are of value only when they agree with the clinical diagnosis."

This astonishing quotation from a modern paper shows the present scientific deadlock in the clinico-pathological concept of osteoarthritis.

The relation of osteoarthritis to aging is also very confusing. According to the curve (Table I, adapted from Junghanns<sup>16</sup>), the frequency of osteoarthritis of the spine increases with age, so that everyone is likely to be affected with this disease in the sixth decade of life. Junghanns' opinion is supported by the majority of writers on this subject. There are, however, authors who disagree with the tendency to make every aging person osteoarthritic. As far back as 1877, Weichselbaum<sup>24</sup> pointed out that it is wrong to consider all bone changes in aging man to be pathological. He asserted that there are bone and tissue changes typical only of aging. Also, in the modern literature we find authors who support Weichselbaum's view, e.g. Albright,<sup>1</sup> Bick,<sup>6</sup> Cobb,<sup>12</sup> Cowdry,<sup>14</sup> Veraguth<sup>23</sup> and others. Although all the above authors

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Based on a paper read at the meeting of Quebec Society for Orthopaedics and Traumatology, November 19, 1955.

TABLE I.—FREQUENCY OF SPONDYLOSIS DEFORMANS IN MEN AND WOMEN IN VARIOUS AGE DECADES (H. JUNGHANNS)



described changes in bone and soft tissues due to aging very thoroughly, they do not attempt to draw a borderline between the normal and pathological in roentgenographical and other signs of the aging process.

As already mentioned, in osteoarthritis the bone changes are accompanied by several, mostly degenerative, changes of soft tissues. Because of this degeneration, osteoarthritis is called degenerative osteoarthritis, degenerative joint disease, and other similar terms by some authors (see Comroe's *Arthritis*<sup>13</sup>). The adjective degenerative does not explain, however, either the etiology or the pathological anatomy of osteoarthritis. In his *Textbook of Pathology*, MacCallum<sup>19</sup> writes the following about degeneration:

"The term degeneration is usually employed to indicate the effect of an injury sufficient not to cause a death of the cell but to disturb its metabolism to such a degree that the raw material or the products of its activities accumulate in it. . . . It would seem desirable, if possible, to abandon the term degeneration entirely and to use others which refer more accurately to the disturbance in metabolism or to the actual injury of the cell. But even if attempted, it would probably be unsuccessful, for the words are so deeply rooted and express so concisely a complex and obscure idea."

The term degeneration is still more misleading when applied to the process of aging. There is no doubt that the aging changes in bone are accompanied by degeneration of cartilages, synovial membranes, etc. It would be wrong, however, to consider such a degeneration as a sign of disease typical of bone aging. In 1942, Bennet, Waine and Bauer<sup>5</sup> published results of the examination of knee joints in persons of various ages who had died incidentally. These authors found that the first signs of degeneration appear as early as in the third decade of human life. According to their data, there is only a quantitative difference between the degeneration found in a man of 30 and that of an octogenarian. Conclusions of Bennet *et al.* were later confirmed by other authors. Thus the degeneration of soft tissues including cartilage is no prerogative of old age alone. Therefore, such a degeneration is neither the cause nor the consequence of bone changes in old age.

In view of this controversy, we decided to undertake a morphological study of bone aging, and especially a study of the relationship between bone aging and osteoarthritis. This study began in 1951 and was at that time supported by a grant from the Atkinson Charitable Foundation. It is now supported by a grant from the Canadian Rheumatism and Arthritis Society.

#### MATERIAL AND METHODS

Five hundred inhabitants of Homes for the Aged in Ottawa and ambulatory patients have been repeatedly examined since 1952. Around 560 skeletons from collections of the Western Reserve University Medical School in Cleveland, the University of Toronto and the University of Ottawa have been used for this study. Skeletons (mostly spines) of 15 dogs in the second decade of life have also been examined, and finally, several bones of cats and rabbits.

Individuals of both sexes, mostly over 60, were chosen for this study.

Hands (i.e. phalanges, metacarpal and carpal bones, carpo-radial joint) and elements of the vertebral column have been the principal subject of examination up to the present but we have recently also started the examination of other joints.

In living persons, the following clinical signs were considered along with the collection of usual anamnestic data: posture, constitution, amplitude of joint movements, tenderness of spine and joints during movements, walking, etc.

Two principal methods were used for this study: macroradiography (synonyms: radiography, roentgenography) and historadiography (synonyms: historoentgenography, microradiography, microroentgenography). Macroradiographs in various projections of x-rays and in different positions of patients and dead material were repeatedly made of all bones and joints mentioned above.



Dead bones were also examined by historadiography. In preparation for this method, genuine (undecalcified) bone is cut into pieces of various thicknesses after embedding in plastic. Bones are now sectioned with a special bone microtome made for this purpose by the R. Jung Co. in Heidelberg, West Germany. With this microtome it is easy to get slides of 5 micra and up. The material is embedded by a method recommended by Bélanger and Bélanger.<sup>4</sup> Slides of bone are put on a special fine grain emulsion with which Eastman Kodak plates 649-0 or Gevaert Lippman T.V. films are coated. Radiography of bone slides is performed by soft x-rays (10-12 kV.). After the usual processing, historadiographs are studied under the ordinary microscope at various magnifications.

spected or palpated. It is quite justifiable, in our opinion, to regard these aging persons as "asymptomatic".

Macroradiographs of all these asymptomatic persons revealed, however, some radiographic signs, which, as mentioned before, are generally considered typical of degenerative osteoarthritis.

All radiographic signs observed by us in aging asymptomatic persons might be divided into



Fig. 1.—Macroradiographs of manubrium sterni with clavicle heads at different ages. (Left to right: male 28, female 48, male 70). Progressive decrease in calcium content with age is conspicuous. (All reproductions of this article are original negatives, therefore decrease in calcium content is manifested by darker colour and increase in content by lighter one.)

The advantage of historadiography in the study of bone is obvious: it permits the study of genuine, undecalcified bone. There are, indeed, many bone conditions which are only characterized by increase or decrease in the amount of calcium. These deviations in calcium content cannot be investigated by the usual histological method, since this requires previous decalcification of bone with all the drawbacks of the latter process. The disadvantage of historadiography is that it is not at present possible to achieve a magnification of more than  $\times 300$ . The technique of historadiography is, however, improving as each month passes, and there is no doubt that greater magnifications will soon be possible. The technique of historadiography has been thoroughly described in the papers of Barclay,<sup>2,3</sup> Bohatirchuk,<sup>8-10</sup> Clark,<sup>11</sup> Egström,<sup>15</sup> Lamarque,<sup>17</sup> Mitchell,<sup>21</sup> Sievert<sup>22</sup> and others.

Gross pathology of autopsy material (preferably of spines and hands) has been studied in several cases.

Macroradiographic and historadiographic studies of skeletons of the above-mentioned animals have been made only with dead material.

## RESULTS

It was found that between 60 and 70% of old people examined did not complain of any bone and joint ailments. These people considered their muscular stiffness, relatively quick fatigue, limited amplitude of joint movements, even occasional pain or discomfort during these movements, to be quite normal and a necessary attribute of their age. At any rate, these people never complained to a physician about these symptoms, and their bones and joints did not present any obvious abnormalities when in-

two categories: atrophic (osteoporotic) and hypertrophic (called by some authors osteosclerotic).

Calcium decrease in bone was observed in aging people in the sixth decade. In the seventh decade osteoporosis became quite conspicuous, i.e. not only was x-ray absorption in bones diminished but also morphological signs of bone atrophy came to view. The number of trabeculae diminished, compact bone was thinned and small cavities in spongy bone appeared. Evidently the atrophic process in aging bones progresses very slowly, because even in the tenth decade of human life we have observed bones which apparently did not lose more than 15-20% of their calcium content, i.e. that content typical of an adult bone. This aging bone atrophy is apparently an irreversible process because we have not seen a single case in which the previous content of bone calcium could be restored by any known means. Women in the study presented a more conspicuous picture of osteoporosis than men (Fig. 1).

A similar atrophic process was found in bones of aging dogs, the only difference being that in dogs bone atrophy was observed earlier (in the second decade of life).

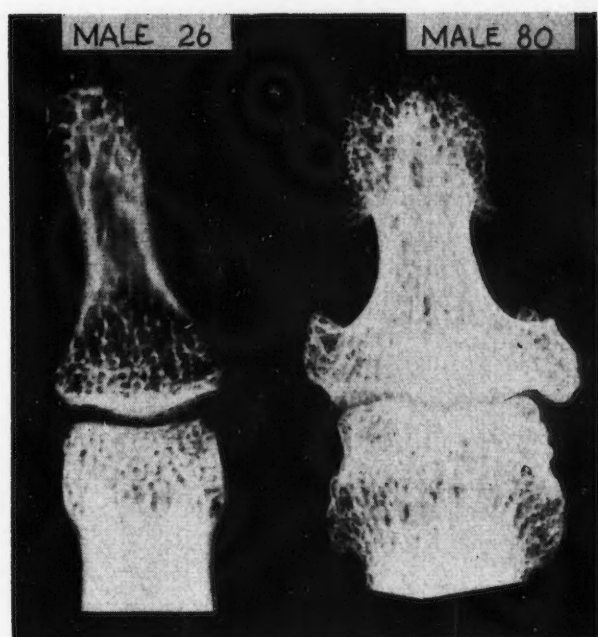


Fig. 2.—Macroradiographs of end phalanges of young (26) and old (80) men. Explanation in text.

Bone hypertrophy was observed in radiographs of bones of all persons late in the fifth decade, sometimes even earlier. The roughness and unevenness of outlines were the first radiographic signs; exostoses and small lippings came to view in later life. The "mushroom sign" described by us<sup>9</sup> was found, as well as calcifications in tendon attachments, rib cartilages, etc. (Fig. 2).

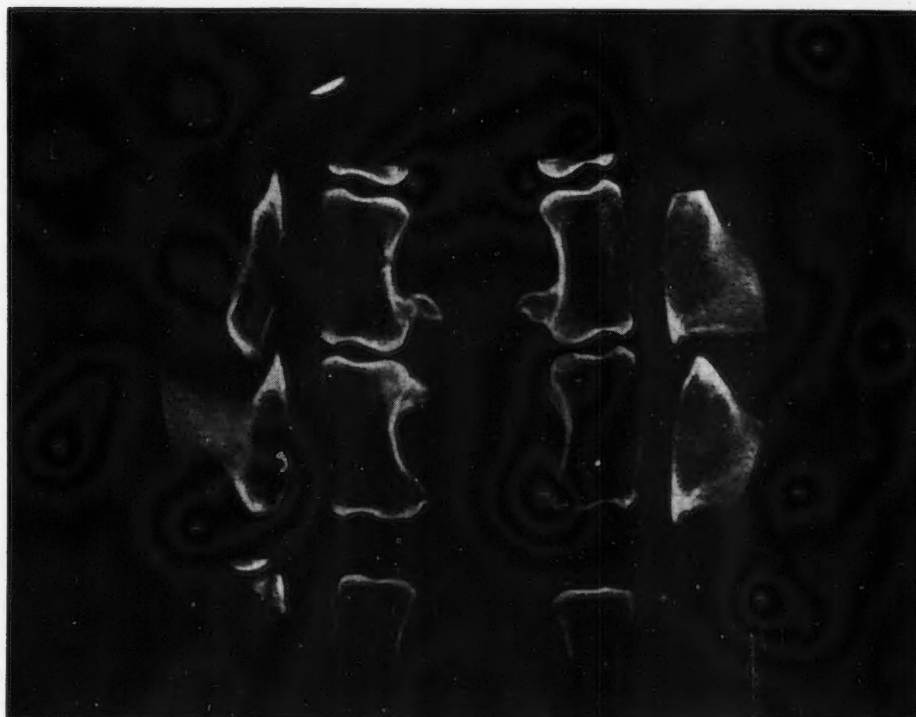


Fig. 3.—Macroradiograph of hypertrophic and atrophic changes in vertebrae of an aging dog.

Similar hypertrophic bone changes were also encountered in dogs in the second decade of life (one or two years earlier than atrophic changes) (Fig. 3).

Atrophic and hypertrophic processes developed in normally aging bone about equally, or else with one of the two processes slightly predominating, but we have never observed such an obvious disproportion between atrophy and hypertrophy in normal bone aging as we have seen in pathological cases (see below).

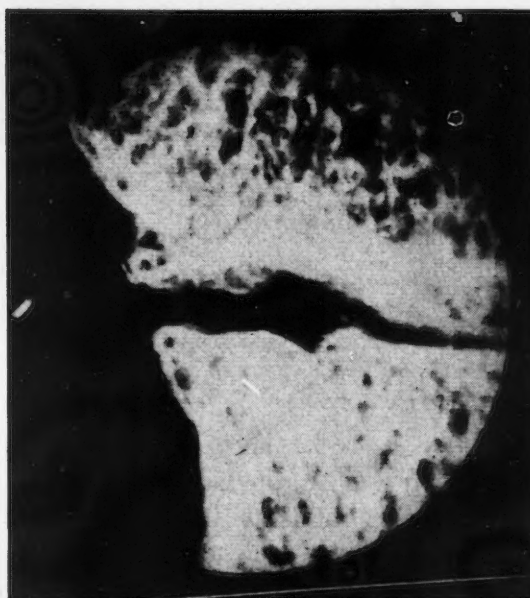


Fig. 4. — Macroradiograph of pathological osteophytes in phalangeal joint.

In contrast with normal aging signs, described above, some of the old persons had radiographic changes in their bones and joints which we consider to be pathological. The majority of these also had such symptoms as permanent pain, very considerable rigidity of spine and joints, swelling in the area of joints, or Heberden and Bouchard nodes. We say "the majority" because a minority of these aging persons had no conspicuous clinical symptoms



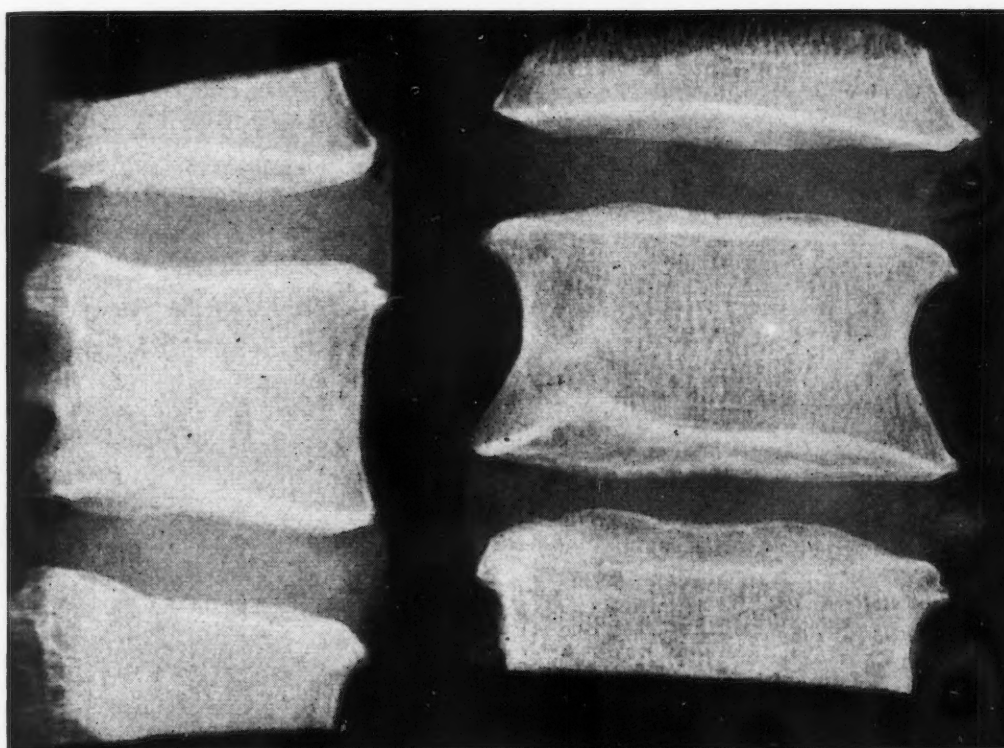


Fig. 5.—Macroradiographs of vertebral bodies in man of 70. Disharmony between the development of prevailing atrophy and hypertrophy is conspicuous. The initial stage of compression fracture with calcium impregnation in the middle part of the vertebral body is seen.

despite quite obvious morphological changes in bones. The previously cited opinion of Lowman<sup>18</sup> is evidently applicable to these people with a demonstrable disproportion between clinical and radiological signs. Aging persons with

pathological signs we propose to call "symptomatic". These signs may be clinical plus morphological, only clinical, or only morphological.

In these "symptomatic" persons the following roentgenographic signs were found.

(a) Much more pronounced lipping than in normal aging people. In advanced cases, even complete fusion of neighbouring lippings was encountered (the latter fusion has been found more frequently in the vertebral column).

(b) Exostoses were observed not only at the periphery of the epiphysis but also in the area of the joint surface. We call these abnormally placed exostoses "pathological". Deposits of calcium salts were often seen on the periphery of such exostoses. Outlines of pathological exostoses (called "osteophytes" by some authors) are mostly irregular (Fig. 7).

(c) Numerous calcifications were seen in intra-vertebral discs, joint cartilages and joint capsules. In contrast to normal aging, we have never observed extensive calcification of rib cartilages in pathological cases.

(d) Disproportion between bone atrophy and bone hypertrophy was quite conspicuous. In cases with prevailing hypertrophy, bone atrophy either did not develop at all or developed very



Fig. 6.—Historadiograph (X 35) of adult bone.

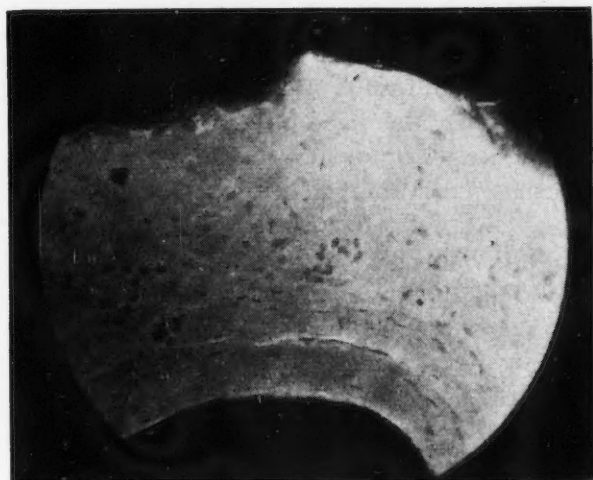


Fig. 7.—Historadiograph of aging bone ( $\times 256$ ); confluent intraosseous lacunæ in the centre of the picture.

moderately. The reverse picture was observed in cases with prevailing atrophy (Fig. 5). In a few cases of extreme osteoporosis, x-ray absorption by bones was equal to that in surrounding soft tissues (so-called "papyraceous" bones). Patients with such osteoporosis (mostly women) were bed-ridden and had very pronounced symptoms. Some authors prefer to separate this group of extreme osteoporosis into a special nosological entity, calling it "senile osteoporosis" (Black *et al.*,<sup>7</sup> Marum<sup>20</sup>). In such cases we have seen excessive decrease in the number of bone trabeculæ, and almost complete disappearance of compact bone simultaneously with development of big cavities in spongy bone. In some cases, compression fractures (mostly of vertebral bodies) were found (Fig. 5).

Historadiographs show no considerable difference as regards x-ray absorption between

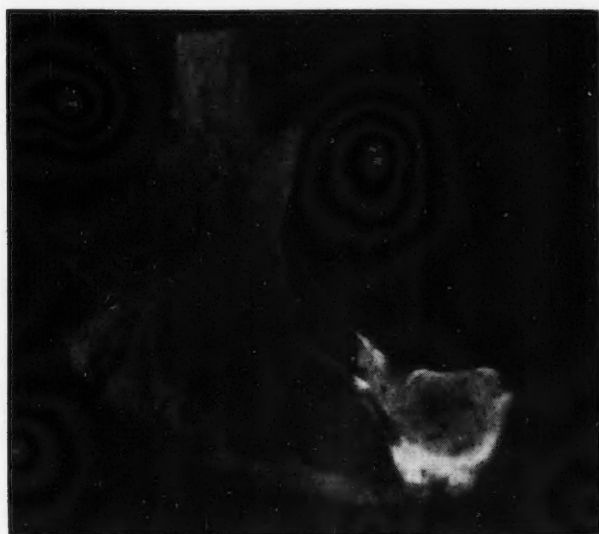


Fig. 8.—Historadiograph of normal lipping ( $\times 120$ ). Explanation in text.

adult and normally aging bone (Figs. 6, 7). The decrease in calcium content especially in the initial stage of aging atrophy is usually detectable only photometrically. As has been pointed out in our previous publications,<sup>9, 10</sup> historadiographs present, however, quite a typical morphological picture in the case of aging bone atrophy: an increase in size of intraosseous lacunæ, resulting sometimes in fusion of neighbouring lacunæ, a much more pronounced bone destruction around Howship's lacunæ than in adult bone; sometimes even almost complete decalcification of some trabeculæ. The enlarge-

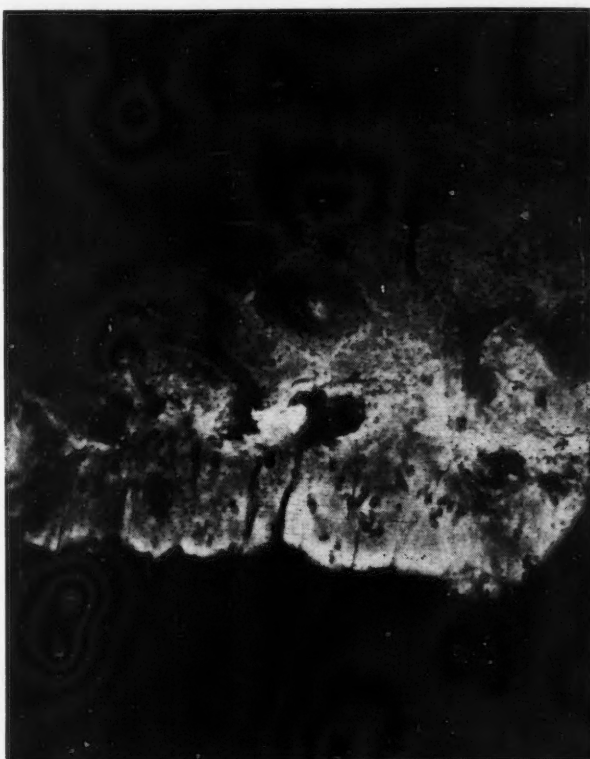


Fig. 9.—Historadiograph of bone ( $\times 120$ ). Two cavities impregnated with calcium are conspicuous (seen as structureless, white).

ment of intraosseous lacunæ in cases of bone atrophy is especially important for understanding the mechanism of bone atrophy. This observation brings forward again the old theory of halisteresis which emphasized the role of the intraosseous lacunæ in this mechanism.

In normal aging, a picture is seen in historadiographs of an area of exostosis or small lipping. Here the bone tissue seems to constitute an entity with the main bone. Identical structures of bone laminæ, intraosseous lacunæ, and the same type of bone canalization are seen, indeed, in exostosis, initial lipping and principal bone (Fig. 8).



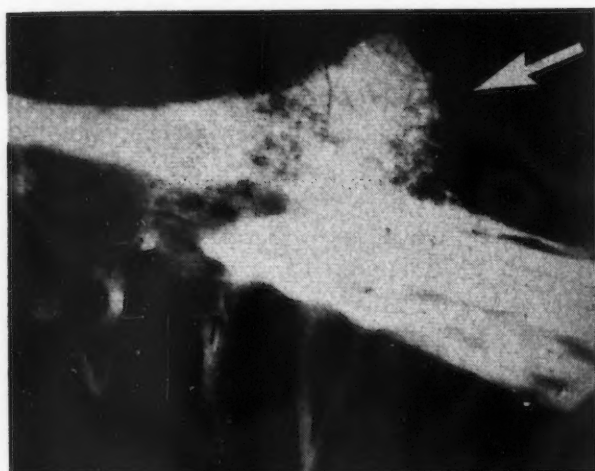


Fig. 10.—Historadiograph ( $\times 50$ ) of pathological exostosis (arrow).

Another historadiographic picture was observed when the process was pathological. The following details were seen in such cases:

- (a) Much more conspicuous bone decalcification.
- (b) Formation of large cavities.
- (c) Impregnation of cavities with calcium salts (Fig. 9).

Where extensive calcification had taken place, bone structure was not present (Fig. 10). In pathological cases, the accumulation of calcium was also seen in the periphery of structurally normal exostosis.

Historadiographs of bones of aging dogs did not differ from those in aging humans (Fig. 11).

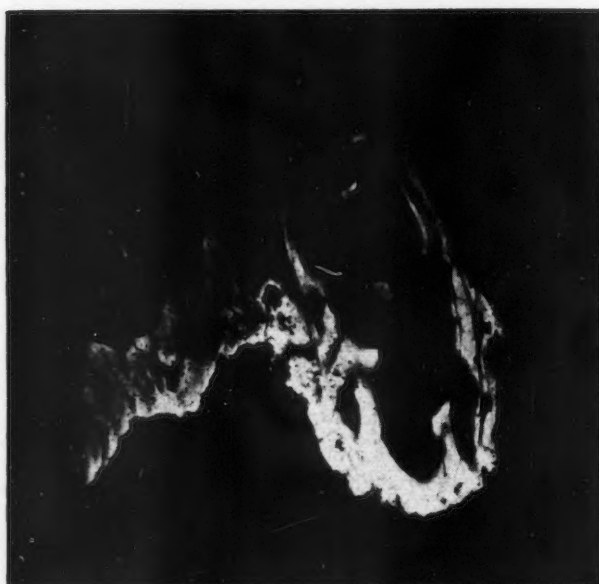


Fig. 11.—Historadiograph ( $\times 35$ ) of exostosis in spine of an aging dog. The identical structure in main bone and in exostosis is shown.

#### DISCUSSION OF RESULTS

Though we do not consider our research completed, the results so far obtained permit us to emphasize the need for differentiation between changes in bones during normal aging and those resulting from pathological conditions. The term "osteoarthritis" may be retained, in our opinion, only for cases where clinical and radiographic signs of pathology are present. We suggest a scheme for differential diagnosis between the normal and the pathological (Table II), based on our findings. In this scheme we use the term "osteoarthritis" for a large group of pathological bone processes resulting in bone destruction or bone deformation. There is no doubt, however, that many of these processes have different causes—trauma, infection, etc. Therefore it is quite possible that in the near future, instead of one term "osteoarthritis", many entities will be distinguished, having various names. One example of such a differentiation is the abovementioned senile osteoporosis. It is not the aim of the present article, however, to analyze all the possibilities of this differentiation.

The similarity of aging changes in bones of man and dog supports the views of those authors who consider hormonal disturbances in old age to be the principal cause of aging changes in tissues and organs, in particular those in the skeleton. Our results give no support to the views of those who consider the weight of the body, due to erect posture, the main cause of development of hypertrophic changes in old age.

Nowadays, we often speak of "physiological or normal old age". We have, however, no exact definition of the condition of human organs and tissues which may be held typical of this normal old age. Our research is an attempt to draw a line between the normal and the pathological in bone aging. This borderline has not only a theoretical but also a practical importance. It is necessary to relieve a normal old man from the psychological burden of a diagnosis of osteoarthritis whenever possible. Here is but one example of this necessity. In the case of normal bone aging, physical exercise alone may delay the progress of bone changes; nevertheless the physician, afraid of the complications of a non-existing osteoarthritis, advises complete rest and special therapy for a normal old man.

TABLE II.—RADIOGRAPHIC SIGNS OF BONE CHANGES IN NORMAL AGING AND OSTEOARTHRITIS

	Normal Aging	Osteoarthritis
Bone Atrophy or Osteoporosis	<p><i>Change in x-ray absorption:</i> Moderate increase in bone transparency, quite conspicuous in the late sixth decade; maximum atrophy in late eighth decade; later on, the progress of atrophy is slowed. Harmonious development of atrophy and hypertrophy in whole skeleton.</p> <p><i>Change in x-ray morphology:</i> Gradual thinning of compact bone, especially in areas of metaphysis and epiphysis. Slight diminishing of amount of trabeculae in spongy bone. Sometimes small cavities in spongy bone (more frequently in vertebral bodies).</p>	<p><i>Change in x-ray absorption:</i> Advanced osteoporosis in earlier decades (sometimes atrophy is conspicuous in fifth decade); faster progress of osteoporosis than in normal aging. Disproportion between the development of atrophy and hypertrophy.</p> <p><i>Change in x-ray morphology:</i> Excessive thinning of compact bone in whole bone, large cavities in spongy bone.</p>
	<p><i>Change in x-ray absorption:</i> In areas of hypertrophy and calcifications (ossifications) increased absorption of x-rays.</p> <p><i>Change in x-ray morphology:</i> Harmonious development of hypertrophy in whole skeleton. Unevenness, roughness of bone outlines; general enlargement of epiphysis and joint surface. Appearance of small lippings and exostoses. Progressive development of rib-cartilage calcifications (ossifications).</p>	<p><i>Change in x-ray absorption:</i> Idem</p> <p><i>Change in x-ray morphology:</i> Disharmonious development of hypertrophy in whole skeleton. Unusual localization of exostoses in separate joints; irregular calcium deposits on the periphery of exostoses; excessive development of lipping, complete or partial fusing of neighbouring lippings (most frequently between lippings of vertebral bodies). Compression fractures. Appearance of calcifications inside bone; development of inordinate calcifications inside joint and in close vicinity to it; signs of bone destruction</p>

To this category of normally aging persons, the wise words of Hippocrates may be applied: "Our natures are the physicians of our diseases—refrain from meddling interference."

#### SUMMARY

1. Macroradiographic and historadiographic data of bone in 500 elderly persons as well as in 560 human skeletons of various ages and bones of aging animals are analyzed.

2. Some bone changes are typical of normal (physiological) bone aging; they cannot be considered as pathological, i.e. osteoarthritic signs. Along with other signs, a harmonious development of bone atrophy and bone hypertrophy is typical of physiological bone aging; disharmonious development of these bone processes is typical of osteoarthritis.

3. A chart for differentiation between the normal and the pathological in bone radiographs is suggested.

4. Historadiography of undecalcified (genuine) bones is recommended for bone studies, especially for those in which the bone content of calcium may be used as a diagnostic sign. Historadiographic findings of bone microstructure in normal bone aging and in osteoarthritis are discussed.

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## RÉSUMÉ

Notre connaissance de l'arthrose est fort imparfaite. La douleur, que tous s'accordent à considérer comme un des symptômes les plus importants, n'a peu ou pas de corrélation avec l'état de dégénérescence osseuse. La radiographie montre souvent des lésions avancées ne causant aucune douleur. Certains auteurs soutiennent qu'il existe des manifestations osseuses typiques de la vieillesse qu'il faut bien se garder de considérer comme pathologiques et d'inclure dans le syndrome de l'arthrose.

L'étude présente porte sur des examens radiologiques multiples de vieilles personnes, et inclut aussi certains

aspects d'anatomie comparée découlant de dissections de vieux chiens, de chats et de lapins. La radiographie microscopique a apporté un concours précieux en fournissant des données qui n'auraient pu être obtenues autrement. Les changements atrophiques du squelette ne s'effectuent que lentement au cours des années, mais semblent irréversibles; les modifications de nature hypertrophique les précèdent. Les lésions pathologiques comprennent les exostoses multiples, la soudure des articulations et la calcification des tissus; l'ostéoporose entre également dans cette catégorie. L'auteur offre certains critères de différenciation entre les processus pathologiques et soi-disant physiologiques. M.R.D.

A FOLLOW-UP ON PEPTIC  
ULCERS\*

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THE PRESENT SURVEY was begun primarily to obtain a follow-up on peptic ulcer cases treated both medically and surgically. Records were reviewed over a specific period of time ending four years before the survey began, so that all cases included in the series had had a diagnosis established for a minimum of four years. Included in the original series were:

1. All cases operated on during this period for cancer of the stomach or ulcer of the stomach or duodenum.

2. All cases showing radiological evidence of ulcer of the stomach or duodenum. (This group included cases showing deformity of the duodenal cap sufficient to make the diagnosis of ulcer presumptive, but in which no definite crater was visualized.)

3. All cases showing abnormalities of the stomach. (These were merely collected for completeness, and no attempt at follow-up was made.)

Such a series unfortunately shows a rather high percentage of cases treated surgically, since a number were referred to the surgeons of the group specifically for operation because of intractability, hæmorrhage or other complications, but no attempt has been made to break down the figures and differentiate cases referred for operation from outside and those originally and continuously treated by the medical department beforehand.

There was a total of 414 patients in the series—324 male and 90 female. The breakdown of cases is as follows:

1. *Duodenal ulcer*—337, with an average age of onset of 36.4 years. (Of these, 28 were 20 years or under in age and the youngest was 12 years; 13 were over 65 and the oldest was 82 years.) Female—71, with an average age of onset of 38 years; male—266, with an average age of onset of 36 years.

2. *Gastric ulcer*—43, with an average age of onset of 48.7 years. (Three cases had both duodenal and gastric ulcers.)

3. *Cancer of the stomach*—18, with an average age of onset of 58 years (two women and 16 men).

4. *Additional miscellaneous lesions*—In all, 16 such lesions were noted by the radiologist: hiatus hernia, 7; duodenal diverticulum, 6; hypertrophic gastritis, 2; congenital abnormality of the duodenum, 1.

## TYPE OF OPERATION

There was a total of 74 operations on 70 patients (female 9, male 61) with duodenal ulcer. Nineteen were for perforations (one patient had perforated twice). Gastric resection was performed 54 times; three of these patients had had previous perforations. Gastroenterostomy was done once. There was one postoperative death, due to acute pancreatitis.

There was a total of 28 operations on 28 patients (20 males) with gastric ulcer—three for perforation and 25 for gastric resection. There were no postoperative deaths.

In cancer of the stomach, all cases had at least a laparotomy.

## REASON FOR OPERATION

*Duodenal ulcer* (70 cases): repeated recurrences or intractability, 32 cases; hæmorrhage, 9 cases; perforations, 18 cases; pyloric stenosis, 10 cases; old gastroenterostomy with stomal ulcer, 1 case. (In many cases there was more than one reason for surgery, such as repeated attacks with periods of intractability, previous

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hæmorrhage, or previous perforation, but as far as possible the predominant one only is noted.)

*Gastric ulcer* (28 cases): perforations, 3 cases; recurrence, 4 cases; hæmorrhage, 3 cases; inability to rule out malignancy either in the first instance or because of unsatisfactory response to medical regimen, 17 cases; obstructive jaundice, thought to be due to carcinoma of the head of the pancreas, 1 case.

#### RADIOLOGICAL DIAGNOSIS

In the case of gastric ulcer and of malignancy, the radiological diagnosis was compared with the final diagnosis, with the following findings:

1. *Gastric ulcer*—36 cases had available x-rays with reports. (a) Correct diagnosis 10. (b) Partially correct 7. (In these cases, the radiologist diagnosed ulcer, but felt that it was likely malignant.) (c) Presumed correct 12. (Ulcer was diagnosed by the radiologist, and either by repeat radiography or by clinical follow-up the diagnosis was presumed correct.) (d) Diagnosis incorrect 7. (In 5, the positive diagnosis of malignancy was made. In one, the x-ray was reported as negative. In one, pyloric obstruction only was reported.)

The accuracy of the radiological diagnosis may be further analyzed as follows: (1) proven correct or assumed correct, 22 (61%); (2) partially correct, 7 (19.5%); (3) incorrect, 7 (19.5%).

2. *Proven carcinoma*.—There was a total of 17 with available x-rays and reports. The diagnosis was correct in 13 (76%) and incorrect in 4 (24%).

The diagnosis in the last four cases was: (1) pyloric obstruction—no cause given; (2) duodenal ulcer with early pyloric obstruction; (3) old duodenal ulcer with scarring; (4) benign gastric ulcer.

Of the 17 cases of carcinoma, 15 had metastases in one or more lymph nodes. One of these patients had survived four years when last seen, but had widespread metastases. Of the two patients in whom no glandular involvement was demonstrated, both were apparently well 5 years and 5 years and 1 month after surgery. In one of these the pathological diagnosis was carcinoma simplex. In the other, adenocarcinoma was found in a small area of an otherwise apparently benign ulcer.

#### TREATMENT

Except in a few instances all cases treated medically were treated as outpatients. The

routine followed with slight variation was as follows.

#### Duodenal Ulcer

1. General discussion. In this an effort was made to give the patient some insight into the condition, and especially the necessity for long-term dieting. The possible complications were discussed and the patient was informed that operation could be performed but that the treatment was primarily medical and a resort to surgery meant a failure on his part or on our part or on both our parts.

2. All patients were begun on a diet of six feedings a day of bland soft foods or milk, feedings being given at regular meal times, between meals and at night. At the end of two weeks, if symptoms had disappeared the patient graduated to a bland diet, still continuing on three extra milk feedings a day. Patients were advised to follow the diet strictly for at least six weeks and thereafter to continue with it as closely as possible.

3. Medication. Usually for the first month, patients were placed on a capsule containing atropine grain 1/150 and phenobarbital grain 1/2 t.i.d., a.c., with antacids usually in tablet form and usually as an aluminium gel preparation between meals and at night. Only rarely were Banthine or similar preparations used and then only on failure of atropine to relieve symptoms.

4. Patients were advised that recurrence was possible and that, if there was a recurrence of symptoms, they were to revert back immediately to their original diet and if necessary to medication.

#### Gastric Ulcer

Diet and medications were as outlined for duodenal ulcer with the following exceptions:

1. The possibility of malignancy was discussed, and the necessity for careful follow-up was stressed.

2. If the clinician or radiologist in the first instance felt that there was a definite suspicion of malignancy, immediate operation was advised.

3. All cases other than those in category (2) above were brought back for assessment and repeat radiography in two to four weeks, at which time a decision was made about continuing medical treatment.

#### QUESTIONNAIRE

A questionnaire was sent out and 143 replies were received. This was rather disappointing, out of a total of 380 cases originally reviewed. However, many of these patients had not been seen for many years (frequently as long as six or seven), and the review took place over those years shortly after the war when there were a great many transients in the city. Fifteen of the patients were known to be dead from other causes; 116 of the questionnaires were returned with address unknown; and 106 did not reply to two questionnaires. Of those who replied, 131 had had a duodenal ulcer, 34 an operation and 97 medical treatment while 12 had had a gastric ulcer (surgical 10, medical 2).

Results of the questionnaire are as follows:



(1)	Total.....	Duodenal ulcer	Gastric ulcer	
	a. Heartburn.....	131	12	
	b. Severe pain before meals.....	100	6	
	c. Food intolerance:	98	5	
	Acid foods.....	84	6	
	Greasy foods.....	100	9	
	Rich foods.....	84	6	
	Other foods.....	36	2	
(2)	How long did you have symptoms before you saw a doctor about them?....	Few days to 18 months; 54 under 6 months	Few days to 4 years; 5 under 6 months	
(3)	Was diagnosis made on your first visit to a doctor complaining of these symptoms?.....	83	6	
	If yes, was the diagnosis confirmed by x-ray at that time?.....	64	6	
(4)	Did you see more than one doctor before the diagnosis was made?.....	46	6	
(5)	Were your symptoms always temporarily relieved by milk?.....	115	10	
	Other foods.....	42	6	
	Antacids.....	75	12	
(6)	Did the pain ever awaken you at night?.....	104	6	
(7)	Were your symptoms worse in the spring and/or fall?.....	61	5	
		(one or both seasons)	(one or both seasons)	
(8)	Could you associate periods of increasing nervous tension or stress?.....	104	8	
(9)	Did your symptoms clear rapidly when you were placed on treatment?...	91	3	
(10)	Did your symptoms only improve on treatment?.....	32	7	
(11)	Have your symptoms recurred since your first treated attack?.....	115	11	
(12)	Did exacerbations of your symptoms respond rapidly on return to your diet, or to diet and medicine?.....	79	4	
(13)	Have you had surgery for your ulcer?.....	34	10	
(14)	If you have had surgery, have you had any return of your symptoms?...	2	2	
		(one perforated again)		
(15)	Do you have to eat small meals since your operation?.....	12	6	
(16)	Do you have to avoid certain foods since your operation?.....	7	5	
(17)	Do you have any other symptoms since your operation?.....	3	4	
		(One had mild flushes following meals. One tired more easily. One developed carcinoma of the pancreas)	(all symptoms minor)	
(18)	How does your present weight compare with that before your operation?			
		Weight decreased	Weight increased	Weight unchanged
	Duodenal ulcer with surgery for perforation only.....	1	1	1
	Duodenal ulcer treated by resection.....	11	3	17
		(4 lost more than 20 lb.)		
	Gastric ulcer.....	6	2	2
		(4 lost more than 20 lb.)		
(19)	Do you do the same work as you did before your operation?.....	30	9	
(20)	Since your operation, do you enjoy social entertainment, such as going out in the evening?.....	34	5	

## SUMMARY AND CONCLUSIONS

1. A series of duodenal and gastric ulcers and carcinomas of the stomach have been reviewed. Figures compiled from the whole series again confirm the well-known facts that all three conditions occur predominantly in the male, and that peptic ulcers are not peculiar to any age group.

2. Out of 337 cases of duodenal ulcer, operation was performed on 70 cases, or 21%; this is considered a high figure but we feel that it is undoubtedly accounted for by the fact that a proportion of the cases had been referred by other practitioners directly to the surgeon.

3. Out of 43 cases of gastric ulcer, 28 (65%) had an operation. In 18 of these cases, either it was not felt that cancer could be ruled out completely at the first visit or there was inadequate radiological response to a medical regimen. In other words, if cases of possible malignancy are discounted, there were 10 cases (23%) treated surgically; this compares with the percentage subjected to surgery for similar complications in duodenal ulcer.

4. The percentage of error in x-ray diagnosis in both benign and malignant lesions of the stomach is noted. This is not in any way meant to detract from the importance of this aid to

diagnosis, but rather to emphasize again the fact that it is only an aid. The patient must be viewed as a whole, and we must not depend on one diagnostic tool to give us a final answer.

5. The questionnaire confirms the well-recognized symptoms of peptic ulcer, its seasonal variations and its tendency to recur.

6. It is noted that 126 (88%) of those patients who replied had had recurrences of their symptoms. Superficially this does not seem to speak too highly for the generally accepted teaching that the treatment of peptic ulcer in the absence of complications is essentially medical. However, the answers to Question 12 show that 83 (61%) of those having recurrences have prompt relief on a return to diet or diet and medication. It would appear, then, that in these patients recurrences are of short duration and easily

controlled by this same treatment. None the less, as long as ulcers tend to recur and humans tend to forget, our treatment will leave something to be desired.

7. Gastric resection in selected cases would appear to be an excellent low-risk procedure. Of the 44 surgical patients who replied to the questionnaire, three had had a closure of a perforation only. Of the remaining 41, only three stated that they had had any return of symptoms. Only eight were more than 20 lb. below their previous weight and most performed the same work as before operation. A percentage ate smaller meals and a few had to avoid certain foods, but none of them considered this a hardship. In addition, many of these patients added a note to the questionnaire, expressing their entire satisfaction with the results of surgery.

## PRELUDIN\* (PHENMETRAZINE) IN THE TREATMENT OF OBESITY

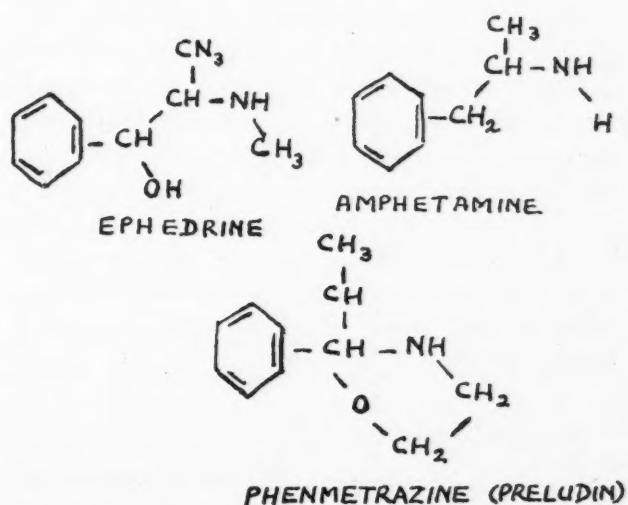
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During the past few years, the therapeutic armamentarium of obesity has been enriched by the contribution of a certain number of drugs liable to reduce the appetite. These products, all dextrogyre derivatives of amphetamine, are all drastic sympathomimetics. They are commonly called "psychamines" because of their action on the psychism of obese patients.

These products, unfortunately, being strongly appetite-depressant, instigate reactions in patients that are very often distressing: tachycardia, nervousness, insomnia, hypertension, dizziness, nausea and perspiration.

In the course of researches on symptomimetic agents, Thomae and Wick<sup>1</sup> succeeded a few years ago in finding the formula of a product chemically related to amphetamine, possessing all the appetite-depressing properties but without toxic effects. This chemical product, Preludin A66 (phenmetrazine) has been in use abroad for a year and possesses a chemical for-

mula very similar to those of ephedrine and amphetamine, as can be seen from the following formulæ:



Preludin, an oxazine derivative (2-phenyl-3-methyl-1,4-oxazine), belongs to the phenyl-alkylamine group.

It has been proven experimentally that the action of Preludin is 1000 to 1500 times weaker than that of adrenaline (epinephrine) but more prolonged. Although Preludin has a central action 5 to 10 times weaker than that of d-amphetamine, it increases cerebral activity in

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an obvious manner. For a few months, we have been evaluating this new drug in the treatment of obese patients. This study concerns 118 patients divided up as follows:

<i>Females:</i> .....	103
under 16 years .....	17
pre-menopausal patients .....	68
post-menopausal patients .....	18
<i>Males:</i> .....	15
under 16 years .....	13
adults .....	2
	<hr/> 118

Of this total, 103 patients have been followed up at the office; the other 15 patients were in hospital.

In order to eliminate error and render the interpretation of the results obtained more rigorous, we made use of the double blindfold method. This method consisted in giving alternately and without the knowledge of the patients two kinds of tablets of identical appearance, of which one contained the active ingredient, Preludin, and the other a harmless inactive substance.

All the patients who were the subjects of this study were put on a diet yielding about 1000 to 1200 calories. So far as possible, variations in weight and reactions to the drug were studied and analyzed at least every fortnight.

The purpose of this study was to investigate the reaction of patients to Preludin. Our attention was centred principally on the following points: variation in weight, blood pressure, pulse, blood sugar level, basal metabolic rate (B.M.R.), diminution in appetite, and length of action of the drug. We also wished to determine whether this drug could provoke a general feeling of anxiety or toxic effects.

#### APPETITE-REDUCING EFFECT

In the 118 patients studied, Preludin has brought about a clear and rapid reduction of appetite. This restraining effect on appetite was so obviously intense in certain patients that the therapeutic dosage had to be lowered. Eight patients reported that the drug lessened their appetite to the extent that they had a real aversion for food. In general, the majority of patients admitted that Preludin controlled their appetite sufficiently for it to help them to adhere more easily to a strict diet.

We would also like to report a most interesting fact. Approximately 25% of our obese patients treated with Preludin stated that after two to three months of treatment with this drug they had acquired, without effort, a certain training as regards dietary restrictions and could subsequently manage without the drug.

Of all the patients in this study, only two reported that Preludin had in no way reduced their appetite. Two other patients told us that dextro-amphetamine controlled their appetite better than Preludin.

#### DURATION OF ACTION

Preludin lessens appetite on an average for 5 to 6 hours, this effect being manifest 20 to 30 minutes after ingestion. Most patients treated previously with amphetamine derivatives stated that Preludin was the first drug that regulated their appetite until bedtime.

#### EFFECTIVE DOSAGE

At the start of our study, we advised our adult patients to take one 25-mg. tablet of Preludin  $\frac{1}{2}$  hour before each meal, but we soon realized that we could obtain the desired results with half this dose and finally adopted as optimal dosage the following prescription: one tablet at 10 a.m. and one at 4 p.m.

This dosage gives the following results: The tablet taken at 10 o'clock in the morning controls the hunger that most obese patients feel by the end of the forenoon; this restraining action extends to mid-afternoon. The second tablet taken at 4 p.m. acts in the same manner for the latter part of the day.

Certain patients treated with Preludin had previously been in the habit of taking a snack, sometimes generous, at the end of the evening. In certain cases, where the loss of this habit became difficult, it became imperative to give  $\frac{1}{2}$  tablet of Preludin at about 9 p.m. to free them from this impulse.

#### MODE OF ACTION OF PRELUDIN

In patients observed for a few years and treated with amphetamine derivatives, we had noticed that these drugs would suddenly arrest the appetite and created a state of satiety in the course of the meal. With Preludin, we have observed that patients lose their appetite even before starting the meal. Many obese patients

have even told us that with this drug they would sometimes forget to eat.

It is impossible to determine precisely whether Preludin acts electively on the appetite-regulating mechanism, or by an indirect action on the mind of the obese. The feeling of well-being that this drug promotes is certainly of tonic value to obese patients who "very often are weak-willed, passive individuals, inclined to find in food very often compensatory satisfaction" (Alexandre<sup>2</sup>).

#### LOSS OF WEIGHT

With Preludin tablets and a dietary regimen, the patients in general lost 7 to 10 pounds a month. In obese patients followed up approximately for four months, we have been able to confirm that this same rate of weight loss is maintained even if the treatment is extended for many months.

#### BLOOD PRESSURE

As the activity of Preludin on blood pressure is approximately 1/1000th that of adrenaline, we can give it without danger to hypertensive and cardiac patients. In all the patients observed in this study and whose blood pressure was regularly controlled, we have never seen any major variation in the blood pressure.

#### EFFECT ON THE BLOOD SUGAR LEVEL

In a great number of patients, we frequently determined the blood sugar level during treatment, and found that Preludin in no way affects this.

#### EFFECT ON THE PULSE

As opposed to amphetamines which so often provoke tachycardia, Preludin causes no acceleration of the pulse. In ten obese patients we even observed a slowing of the pulse rate during treatment, although they were taking 75 mg. per day.

#### STUDY OF TOXIC EFFECTS

As we had previously observed with other sympathomimetic drugs certain vasomotor disturbances such as excitement and sometimes real psychoses, we have closely studied the nervous reactions and mental behaviour of patients treated with Preludin.

A study of our data permits the statement that 99% of our patients treated with Preludin remained free of all signs of nervousness and had no palpitations or insomnia. Many patients who had previously not been able to take amphetamines without the distress of persistent nervousness felt no such effect with Preludin. One of our patients, who for a few months was in a constant state of nervous tension after habituation to 4 or 5 tablets of amphetamine a day, admitted that she was able to control her appetite with only 2 tablets of Preludin a day. She was proud of the state of serenity and calmness she was in with this drug.

#### SIDE-EFFECTS

During Preludin treatment, a few patients mentioned an occasional bad taste in the mouth. Ten patients reported that the drug caused a disagreeable dryness of the mouth. Two patients had to cease treatment because of the persistence and intensity of this discomfort. But in general a reduction to half the dosage was sufficient to suppress this symptom rapidly.

One patient complained that Preludin produced a sensation of euphoria; another blamed the drug for causing abdominal cramps. Four patients reported an unusual symptom in the course of treatment. They complained of feeling sad; they felt "like crying" and "had the blues".

During this study with Preludin, we have given special attention to reactions that could be present in four groups of obese patients: children, adults without hypothyroidism, hypothyroid patients, and women after the menopause.

1. *Children.*—Obesity in children constitutes a complex problem where numerous nervous, psychic, and somatic factors intervene. The endocrine factor is insignificant and of little importance in the pathogenesis of obesity in pre-puberty and in puberty. In 90% of cases, the fundamental cause is the food factor. This is the type of simple obesity, the obesity of luxury. In the child, there exists a second factor in the genesis of obesity, the psychological factor. In fact, most obese children have a particular emotional and psychic behaviour. They usually lack maturity from the social and emotional point of view.



From the start of our experiments with Preludin, it has seemed that this drug could satisfy the double requirement in the treatment of children—correct their gluttony and improve the psychiatric outlook. Compilation of the charts of 30 children, whose ages varied between 4 and 16 years, has confirmed this first impression.

Preludin is marvellously well tolerated in children at a dosage of  $\frac{1}{2}$  tablet twice a day. This drug greatly lessens appetite; it increases the physical capacity in intensifying the desire for activity. Moreover, it gives an impression of well-being, improves the psychiatric outlook and makes the rigours of dieting more acceptable.

2. *In adults without hypothyroidism.*—Of the adults observed in this study 82% had a normal basal metabolism. This confirms the opinion that hypothyroidism is not the factor usually responsible for obesity in adults. In these euthyroid patients, diet associated with Preludin therapy is sufficient to bring about a clear therapeutic result.

3. *In hypothyroid adults.*—Of 88 obese adults observed in this study, 18% had a low basal metabolism and clinical signs of hypothyroidism. In these patients, the association of Preludin and thyroid was manifestly better tolerated than all other medications previously used.

4. *In women after the menopause.*—The obesity frequently observed after the menopause is difficult to correct. This obesity, which favours the hips, the buttocks and the nape of the neck, is usually conditioned simultaneously by hydrophilia and cellular lipophilia. This "spongy obesity" stems from vegeto-metabolic disturbances and psychosomatic factors.

Estrogens, frequently used in women at this period, are another factor causing chloride retention, which compromises the effectiveness of all therapy directed to this form of obesity.

In women older than 50 years of age, our experience with Preludin has not been too gratifying. Even with the help of energetic diuretics and strict diet, obesity remains very often refractory to treatment. Our results are the same as those obtained with drugs used previously.

## CONCLUSIONS

Preludin (phenmetrazine) is a valuable auxiliary in the treatment of obesity. Its action, as depressant of the appetite, is rapidly manifest and prolonged.

This drug is marvellously well tolerated, even by children. It is in general free of all toxic effect. It does not cause the excitement accompanied by fear and trembling that we often observe with amphetamine.

Although the euphoric action of Preludin is less pronounced than that of amphetamine, this new drug has excellent effects on mood and increases the power of concentration.

Of all the drugs we now possess to treat obesity, Preludin is probably the first and only one that so well combines powerful action and perfect innocuity.

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## SCIENCE ON TV

"We do not know how much confusion about science is generated in the minds of the television viewers by the ubiquitous pitchman in the white coat, full of 'scientific proofs' and oily admonitions. He relies on gadgets and the use of 'controls', often irrelevant. He may triumphantly demonstrate the efficacy of a deodorant by passing a presumably noxious vapor through a 'smellometer' before and after treatment. Or he may demonstrate the well-known capacity of an acid to eat a hole in a pocket handkerchief and show that addition of such-and-such a product, conveniently available in the form of pills, can neutralize the acid. To anyone who recalls a bit of physiology this is puzzling, for he knows that the stomach contents are normally acid and that the digestive juices operate only in an acid medium. The moral is difficult to draw. It would seem to be that somehow acid is a bad thing to have in your stomach or, possibly, that if you want to eat pocket handkerchiefs, you had better not take such-and-such at the same time."—*Science*, 124: 963, 1956.

## TRENDS IN TUBERCULOSIS\*

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THERE HAVE BEEN TIMES during the last 20 years when attempts to obtain information on anti-tuberculosis activities in Canada have not been welcomed with enthusiasm by either administrators or clinicians. Sometimes it has been classed under the heading of "useless information". Perhaps Will Rogers understood the reason when he said, "Collecting statistics is like collecting garbage. After you have it, you have to do something with it." There always seems to be a feeling that much information is gathered and not used. However, we seem to be on good ground for collecting it, since no less a person than Abraham Flexner, when he was accepting an honorary degree 20 years ago from Bryn Mawr, gave an address on "Usefulness of Useless Information". I like to feel that the benefits which we have derived from efforts to obtain tuberculosis statistics are a demonstration of Dr. Flexner's thesis and, I feel, need no apology.

At a time when the final outcome of the tuberculosis problem is still uncertain, it is pertinent to study some of the trends which are taking place in regard to all phases of the disease. It has been said—and rightly so—that we depend too much on death rates for any conclusions as to what is happening. It is true that death rates have fallen so rapidly that they do not tell the whole story and perhaps give a distorted picture. Unfortunately, statistics dealing with other phases of the problem have not always been available and are not so accurate. They are improving, and when certain factors are taken into consideration, they give some valuable information and can correct some common impressions which are not always accurate.

As far as the deaths are concerned (Fig. 1), there is no question as to the change that has come about. The gradual reduction which has been taking place for some years has become a steeper drop since 1948. In the 20 years from 1928 to 1948, the death rate fell 54%, but from 1948 to 1953, it fell to 10.3—a reduction of

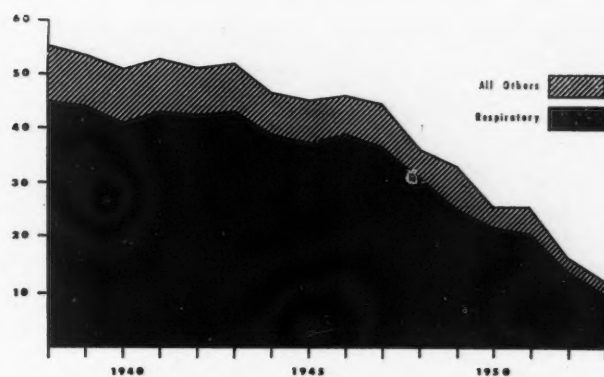


Fig. 1.—Death rates per 100,000 population, for tuberculosis all forms and tuberculosis of respiratory system, Canada, 1938-53.

72% in five years. The reduction is noted both for age and sex, although the older groups have not been so markedly affected and there has actually been an increase in males over 65. The most striking feature has been the disappearance of the peak for young females and the smaller one for the middle-aged male (Fig. 2).

The fall for the different provinces of Canada will be noted (Fig. 3). It will also be noted that there is a tendency for these rates to reach a uniform level. The trend in other countries is observed and it is of interest to compare this with Canada. Our latest figures list in this order the following countries: Denmark, Holland, Canada, United States, Sweden, England and Wales.

### MORBIDITY

The morbidity picture is not so clear-cut, but shows some pretty definite trends. An increase in population since the war and an increase in case-finding facilities have obscured the trend, in that the actual numbers have fallen slowly, as has the greatly accentuated program in the Indian population. In 1944, the figures were 15,292 for new cases reported. This was the peak year. In 1946, the figures were 15,263 and by 1954, they had fallen to 10,404. When notifications are reduced to a rate per 100,000 we have the following: the rate in 1944 was 128.2, in 1946 it was 124, and by 1954 it had fallen to 69.1, a reduction from the peak of 1954 of 46% as compared to a fall of 78% in death rate.

It will be noted that the admission rate for immigrants is falling rapidly and is approaching the first admission rate for the rest of the population. In 1954, it was 71.7 and it was

\*Delivered at the Medical Advisory Section Meeting, Ontario Tuberculosis Association, Toronto, October 27, 1955.

†Executive Secretary, Canadian Tuberculosis Association.



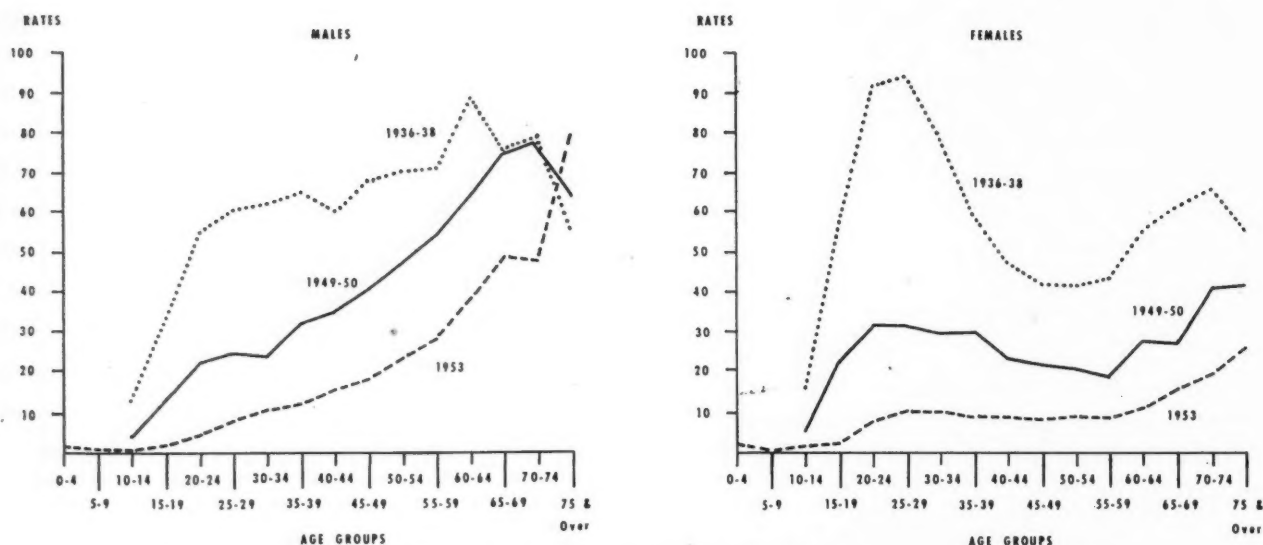


Fig. 2.—Canada tuberculosis death rates per 100,000 population, by age and sex, for selected periods. Source: Annual Reports of Epidemiology and Vital Statistics, 1950, Dominion Bureau of Statistics.

actually lower than for two of our own provinces. The over-all first admission rate is 62.7. This is in keeping with experience in past years. When immigration from Central Europe was at its peak and when the largest percentage of the population of Saskatchewan was foreign-born, that province had the lowest death rate in Canada. Cities in Canada with a high proportion of foreign-born are known to have had some of the lowest death rates of our Canadian cities, whereas the high death rates have tended to be in those provinces with a very high Canadian-born population.

#### TREATMENT STATISTICS

When we come to treatment statistics, we find that there has not been the same fall. We need, however, to consider a number of factors which have complicated the picture. Let us consider the bed complement. It steadily increased as new beds became available until 1953, following which there has been some reduction. The figures for bed complement are as follows: increased from 8,825 in 1938 to 18,977 in 1953; fell to 17,683 in 1954. There will be a further reduction in 1955. The number of admissions, whether they are first admissions or readmissions, is of importance in showing an accurate trend.

*First admissions* increased from 6,429 in 1938 to 9,661 in 1953, falling to 9,523 in 1954. The highest rate per 100,000 was in 1946—77.2—and stands at 62.7 in 1954.

*Readmissions* reached their peak in 1950 with 32.8 per 100,000 and have fallen to 26.7 in 1954. This is significant because of the prediction that with drug treatment, and hence more recoveries, there might also be more reactivations. So far, this has not happened.

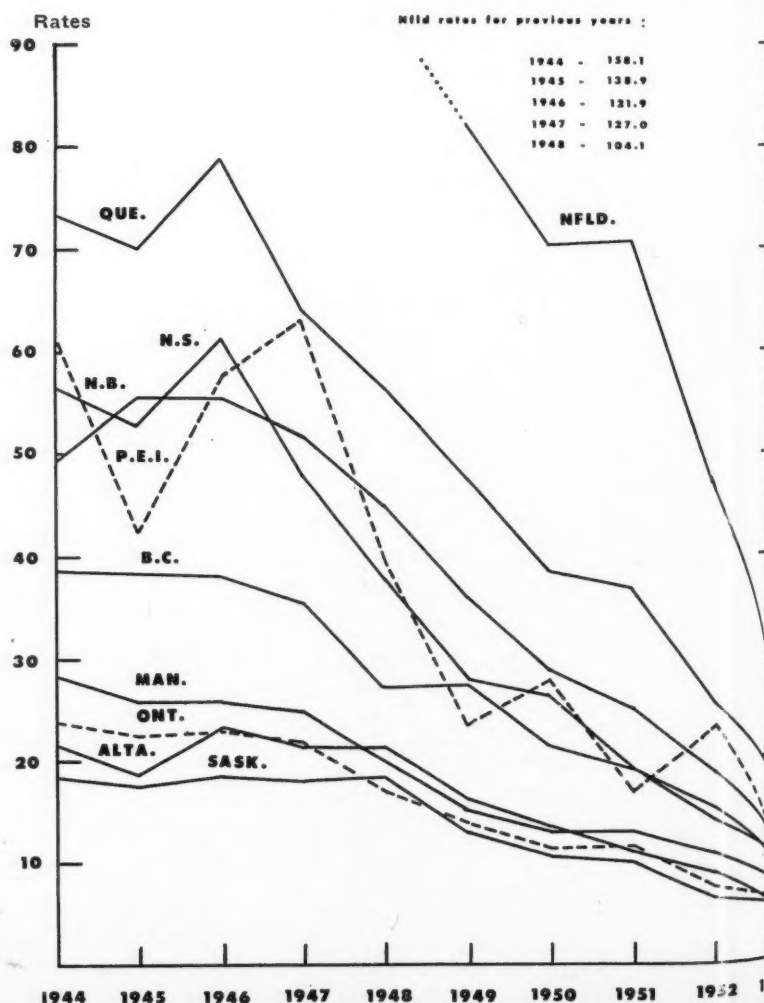


Fig. 3.—Provincial tuberculosis death rates per 100,000 population (including Indians), for selected years. Newfound rates for previous years: 1944—158.1; 1945—138.9; 1946—121.9; 1947—127.0; 1948—104.1. Note: Halfbreeds are included. Newfoundland rates include Indians.

One trend that was evident in 1954 will be watched with interest in future. It is the number of non-tuberculous patients admitted to tuberculosis institutions. The number increased from 1,165 to 2,029 in 1954. While these showed a greater proportion of non-tuberculous pulmonary diseases and lung cancers, the list covered a very wide range of medical conditions. It fitted into a picture of chronic diseases, rather than a disease entity. The range of non-pulmonary diseases would have been greater if the diseases treated in the beds eliminated by the reduction in bed complement had still been included.

*Bed occupancy* is affected by the number of admissions and readmissions and also by the length of treatment. Contrary to general belief, length of treatment has steadily increased during the past four years from 300.9 days in 1950 to 371.9 in 1954. Hence the percentage of bed occupancy has remained at a similar figure for four years (89-90-91.5-92.2). However, at August 30, 1955, it stood at 82%, low even for a mid-summer rate. Will this be maintained? Time will tell!

#### CASE-FINDING

There would appear to be no doubt that case-finding is becoming more comprehensive and the problem is being attacked on a wider front. As far as numbers examined are concerned, there has been a steady increase for many years. The three main groups, for which we have been keeping records, are: (1) clinics and dispensaries; (2) hospital admissions; (3) surveys.

The first group includes suspects and contacts, together with the follow-up of ex-patients. Since it includes most of the patients referred by private physicians, it is obviously the basis of the tuberculosis control program. The number of examinations increased until 1954.

The hospital admission program continues to expand as additional hospitals come under the program. It will continue to be increasingly important. The numbers x-rayed are growing faster than in any other group.

The survey program seems to have reached a peak—around two million of our 15 million population. As long as it gets a good coverage, and particularly as far as the older age groups are concerned, there would appear to be a place for it. But where numbers mean more

than the particular groups examined and where community participation is low and consists mainly of young children, it would appear to be a waste of time, effort and money.

#### PREDICTIONS AS TO THE FUTURE

There seems to be no doubt that tuberculosis as a cause of death will pass pretty rapidly out of the picture. The range of antibiotics is increasing and, while streptomycin and isoniazid are undoubtedly superior to the others yet available, enough variation is possible that the problem of resistance will probably not become as important as we first thought. Morbidity will probably fall more slowly (5-10% a year).

The problem of diagnosis will not diminish. It is, and will continue to be, good business to explore every avenue to foster early recognition and adequate treatment. It is a program which will require imagination and energy. All the features now in use will still continue to be useful. The mass survey, while it may be spaced out, will still be necessary and deserves even more attention as to organization. The surveys which fail to get the maximum participation of the population, and particularly of the older age groups as mentioned previously, are a waste of time and effort.

The greatest changes will come in the matter of medical and hospital services. There will probably be a gradual reduction per year (5-10%) in occupancy by tuberculous cases. This will compel the admission of non-tuberculous cases. While these will include primarily respiratory diseases, the bulk will be other more general conditions, depending on the need in a particular area or province. Chronic diseases in general will likely be the main concern.

This will lead to a change in the type of medical service responsible for medical care of the tuberculous. Failing any comprehensive national or provincial health insurance plan, non-tuberculous patients admitted will be treated by consultant and attending physicians. Already the tuberculosis service is failing to attract the recent graduate or the young physician. If this keeps on, it will mean an aging medical service, which will lack the enthusiasm for teaching or for attracting younger personnel, unless new services and new incentives are provided.

Perhaps the change that came about in the veterans' service could be a pattern for the



future. A good many of us remember that service as it was after World War I and as it was in 1939—an aging clientele with an aging medical staff, which had survived the economy campaigns of the treasury board of the early thirties and which was not too attractive a service. Practically none of the staff had teaching appointments in the medical schools and the service was not recognized for postgraduate training.

Contrast this with the present situation. While those on whom administration falls and some key men are full-time, in the main the staff positions are for part-time consultants who have teaching connections with medical schools. These services are recognized by the Royal College of Physicians and Surgeons for postgraduate training and many of the full-time younger staff positions are occupied by men completing their fellowships in medicine and surgery. Our hospitals could very well follow a similar pattern in most centres.

Some suggestions have been made that they might become hospitals for chest diseases or cardiac services. These do not constitute enough to take up the slack. Neither do I think it desirable to segregate disease entities in the future. It has been successful for tuberculosis but, after all, tuberculosis is an infectious disease. Perhaps also there is a parallel in the disappearance of the old contagious disease hospitals. These are now replaced with infectious wards in general hospitals. The main point here was that the case load disappeared and hospitals were put to other uses. It is true that tuberculosis will disappear much more slowly and the change-over will be more gradual.

If my reading of the crystal ball is correct, this means that we will adopt an entirely different attitude to staff recruitment. It will mean also that staff will need a wider training than ever. Fully qualified junior assistants will be required. No one should be appointed who is not equipped to enter any field of medicine or surgery. Opportunities for training will be part of the service. In the future, senior staff appointments should require certification or fellowship in the general fields of medicine or surgery.

Under such a system, discrepancies in salary will tend to disappear. The salaries of superintendents and directors are not too far out of

line with those of other members of the profession, but the same cannot be said concerning remuneration of junior physicians. Unless more thought is given to those who are to follow, we are apt to find ourselves with serious staff shortages, which will do damage to the cause we seek to serve and to medicine in general.

In a consideration of the use of part-time staff we would do well, I believe, to consider where such services would be *adequate* and where *inadequate*. In what fields are they useful and where are their limitations?

More part-time personnel could very profitably be used in diagnostic and case-finding services. A complete hospital admission program, with outpatient chest clinics, would add to the effectiveness of our present set-up, and I feel sure that this is a sphere in which part-time work could be utilized. This would provide an opportunity for closer contact with general medicine and surgery than is possible in many centres. There should, however, be some overall supervision. At a time when the number of tuberculous ex-patients in the community is greater than ever, it is even more desirable that proper supervision be available. Otherwise, one can visualize the indiscriminate use of antibiotics which might be experienced. It has been our experience that inexperienced staff tend to over-diagnose and over-treat.

It is when we consider the provincial administration and the over-all supervision of clinics and tuberculosis hospitals that we come up against the limitations. This is an area where I believe full-time services are still essential. We are all aware of the impetus given to the fight against tuberculosis by the dedicated men who put their whole energy into the administration of sanatoria and province-wide programs in the past. I do not think such work as theirs would have been possible on any part-time basis. Singleness of purpose gave a drive to their efforts which I am sure would have been dissipated by divided loyalty. It seems to me, therefore, that while we can, and undoubtedly will, use part-time services in many fields, when it comes to supervision of provincial services with over-all supervision of community and industrial surveys, case registers and clinic services for the whole country, full-time staff will be required for many years to come.

The greatly increased number of patients with inactive disease in the community appear to be

standing up well to ordinary conditions of life. Only time will tell whether they will be a source of intermittent infection. At the present time, it would appear that we have reduced the intensity of infection by a fairly adequate system of isolation and efficient treatment. It remains to be seen whether potential sources of infection will not become more widespread than ever, resulting in local epidemics of tuberculosis developing in a tuberculin-negative environment.

#### BCG VACCINATION

To my mind, one of the uncertain points is the part which vaccination will play in our campaign of the future. The experience of thirty years would appear to have established the fact that vaccination is of value in preventing serious disease, which follows very closely a primary infection. It is also a constant observation that meningitis and miliary tuberculosis are exceedingly rare in vaccinated groups. We have a long way to go before we have used BCG adequately in the groups where it is likely to be of life-saving value; that is to say, in contacts, nurses, medical students and groups with a high morbidity and mortality rate. At the present time the Indian Medical Services are making most use of it and with apparently good results. Two provinces have adopted it on a general scale.

A rather disturbing feature at the present time is a tendency to minimize the value of BCG. At the same time the use of isoniazid as prophylactic medication in negative reactors and as prophylactic treatment for primary infection has been mooted. In my opinion there is no proof of the first proposition, and there is divided opinion as to its routine use in the second. There is the problem of the development of resistance, and we have been particularly warned against short-term broken periods of treatment, such as we are likely to have after such a regimen. The wholesale use of other drugs more specific in their action, such as quinine for malaria, has been difficult to carry out. It would require a lot of staff to supervise it properly. One has a feeling that a program such as administering a daily dose of isoniazid, as has been suggested, may be poor public health practice, not established on a sound basis. This seems to emphasize the greater need

than ever for research in regard to immunity and the control of primary infection.

The problem of early discharge and discharge against advice seems to be looming larger and larger in the picture. It arises out of the fact that patients feel well and need continual reassurance and persuasion to remain on treatment. There is also the growing impersonality of treatment. This arises, I think, out of the new tools which enable us to streamline treatment. We are short of staff, so we tend to spread trained services over as wide an area as possible. The doctor does not spend anything like as much time as he did a few years ago with each patient. When we were not able to give a miracle drug, we gave more of our time and the result was a patient-doctor relationship which helped patients stay the course. The confidence they had in their doctor, who, they felt, was a personal friend, helped them withstand the tediousness of institutional life.

The nurse-patient relationship also tends to be changed by modern treatment. It does not take very long to give a shot of streptomycin. The nurse had more time to listen to the patient's problems and talk them over in the day when she gave the bed baths. Now the patient takes his own, or a nurses' assistant does the job.

There is no question of going back to old methods, but can we not make an effort to get back to the warmth and humanity of the pre-antibiotic days? Granted it takes time, and we are busy. But of what avail is that saved time if, in the long run, the patient leaves against medical advice and infects others; or alternatively, is restrained legally—which will probably turn out to be even more expensive and not always successful.

This leads us to a discussion of the whole field of rehabilitation. This is one of the fields of tuberculosis control which is getting more and more attention, but it is not getting too much. It has been said over and over again that we should view every patient as a candidate for rehabilitation, which should be considered as a part of treatment.

I think we should give continuous thought to the cause and try to overcome, wherever possible, the reasons why patients leave the sanatorium against advice. There is no doubt that in many instances the cause lies in boredom and the lack of any planned program for oc-



cupational therapy, physiotherapy or vocational training.

There seems to be a growing demand for legislation to force stay in sanatoria. I am not against such legislation, but I feel very strongly that, when it is necessary, we should feel that there has been a failure somewhere in handling the patient and that we should accept some of the responsibility. If we have such legislation, let us not use it as an easy way out. Let us regret the need for it and determine that we shall do everything we can to prevent the necessity of invoking it.

There are two groups in our sanatorium population that present special problems and for which legal restraint does not seem to me to be the full answer. There is the chronic case, bacillary or intermittently positive. There is also the elderly person now found in increasing numbers in our hospitals. Can we not make some other arrangements for the care of these people? It seems a dreary prospect to me to think of an aging person penned up in a hospital ward. Not much chance of life, liberty and the pursuit of happiness in that!

I know that most institutions nowadays have a policy by which old people are always considered ambulant, but I wonder if we should not try for something with even more latitude, especially for elderly men, since they are such a large group. Some of our institutions should be a hostel type where there could be a homier atmosphere than seems possible in a hospital, even with access to occupational therapy workshops. What I am advocating is the working out of some kind of scheme which will give the chronic a more normal life. I think any efforts we make in that direction would pay off in greater co-operation from them. In my opinion a number of the smaller country rehabilitation centres maintained in England for this purpose are ideal for this type of patient, such as we have been discussing. I am not referring to the colony type, such as Papworth and Preston Hall. While these served their main purpose, which was to direct attention to the great problem of rehabilitation of the tuberculous, at the best they took care of a relatively few people. They created problems in some instances because they segregated families as well as individuals.

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#### RÉSUMÉ

Le taux de mortalité de la tuberculose a accusé une baisse si rapide au cours des récentes années qu'il a peut-être contribué à donner une image un peu faussée de l'état actuel de la maladie. Cependant, un fait important à signaler est la disparition du clocher de la courbe de mortalité chez les jeunes femmes et de celui moins élevé, chez les hommes d'âge moyen. Les taux des différentes provinces tendent à atteindre un niveau uniforme. L'accroissement de la population ainsi que les moyens améliorés de dépistage ont jeté une certaine confusion dans les statistiques de morbidité. Les chiffres n'en sont pas moins encourageants. Le nombre de lits augmenta jusqu'en 1953; il a légèrement baissé depuis; le chiffre des premières admissions a atteint son sommet en 1946 et a décliné par après; les ré-admissions ont fait de même depuis 1950. Il est intéressant de noter que le nombre de malades non tuberculeux admis dans des institutions consacrées au traitement de la tuberculose va en augmentant depuis 1950. La durée moyenne du traitement montre une tendance à augmenter contrairement à ce que l'on pourrait croire. Le service de dépistage prend une amplitude croissante et attaque le problème d'un plus grand nombre de côtés qu'il ne l'a fait jusqu'à présent. Tout semble indiquer que la tuberculose en tant que cause de mortalité disparaîtra bientôt; la morbidité qui s'y attache passera plus lentement; cependant, le problème du diagnostic conservera toute son importance. Les services médicaux et hospitaliers continueront à s'occuper des maladies respiratoires chroniques. On s'aperçoit déjà que la spécialisation en tuberculose perd de sa popularité auprès des jeunes médecins. L'emploi de personnel à temps partiel pourrait être toléré dans certaines circonstances, mais pour ce qui est de l'administration provinciale et du contrôle des cliniques et des hôpitaux, l'auteur insiste pour que ceux qui en seront responsables y consacrent tout leur temps. Il semble que la vaccination par le BCG contribue à la prévention de formes graves de la maladie après le développement d'une primo-infection (méningite, tuberculose miliaire). Le problème du congé prématuré découle en partie du bien-être que ressent le malade sous traitement, et aussi de la dépersonnalisation de ce même traitement. Le rapport qui existait jadis entre le malade et son médecin se perd maintenant parmi le grand nombre de spécialistes contribuant à l'administration de ce traitement. La question de la réhabilitation en tuberculose reçoit une attention croissante, qu'elle mérite d'ailleurs. Elle existe en rapport avec le besoin que l'on ressent dans certains milieux d'avoir une législation s'appliquant au séjour d'hospitalisation. L'auteur est d'avis qu'une atmosphère plus sympathique diminuerait les départs sans approbation médicale et pourrait même obvier à la nécessité d'une telle législation.

M.R.D.

#### CLINICAL TESTS OF THYROID FUNCTION

Russell Fraser (*Lancet*, 2: 581, 1956) discusses the three types of test for thyroid function and compares them on the basis of many thousands of cases. Basal metabolic rate gives the best index of severity of thyroid dysfunction. The radio-iodine test in the absence of previous drugs gives the best test for suspected thyrotoxicosis. Chemical estimation of the level of protein-bound radio-iodine in the plasma is most useful for suspected mild myxoedema, in which results of other tests may be normal.

## PROSTATIC HYPERTROPHY: CHOICE OF OPERATION\*

### A REVIEW OF PERSONAL EXPERIENCE

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EACH SURGEON APPROACHES the subject of prostatic hypertrophy with a different background in training and experience. The topic could be considered in textbook fashion and each operation could be dealt with in a neutral manner by outlining its classical indications but making no attempt to indicate preference. However, there would be small interest in such a recital, and the subject will not be considered from this point of view. The limitations and complications of the various operations will be reviewed as they have affected and changed our approach to prostatic surgery. The observations and comments are based on experience in 2000 prostatic operations which we have done and followed up in the past ten years.

There will be no criticism or comment on perineal surgery. Our experience with this method is insufficient to allow for appraisal of this method of prostatic surgery.

In the early years of prostatic surgery there was a choice only between single-stage and two-stage suprapubic prostatectomy. This period was followed quickly by the development of perineal surgery. During the 1930's there developed an increasing interest in transurethral surgery, and in 1945 there was added the retropubic operation of Terence Millin.

This paper will discuss single-stage and two-stage suprapubic prostatectomy, transurethral resection and retropubic prostatectomy. Our problem is to find the best method to use for the majority of cases of benign prostatic obstruction.

*What are the various factors in determining a choice?*

1. *Mortality.*—In the early years, a few surgeons did suprapubic prostatectomy with a relatively low mortality rate, but in general the mortality was very high. This fact, plus the long morbidity after suprapubic operations, encouraged many surgeons to adopt transurethral resection once the technique was perfected. The

low mortality rate of 1 to 2% in transurethral surgery made the operation very acceptable. Because of the low mortality, we operated on a high percentage of our cases by transurethral resection for many years.<sup>1</sup> However, our experience with retropubic prostatectomy has shown us that this method of open operation can be carried out with as low a mortality rate as in transurethral resection.

2. *Morbidity.*—Two-stage suprapubic prostatectomy is usually accompanied by a long hospital stay and a varying period with a wet sinus. Patients do not like two major operations, and this method is therefore less frequently used. Transurethral resection is not accompanied by an open wound, and the postoperative stay is relatively short.

Single-stage suprapubic and retropubic prostatectomy have grown in popularity. We find the retropubic operation increasingly an answer to the requirements of a total adenectomy with a very low mortality, an early dry wound, and one operation.<sup>2</sup>

### *Major Complications.*

In making a choice, we must have in mind important complications that occur in prostatic surgery. These complications influence the decision as to the best operation. Let us deal with these complications and comment on their importance.

1. *Hæmorrhage.*—The control of primary bleeding in transurethral resection is usually excellent. However, secondary and occasionally delayed hæmorrhage does occur. In single-stage and two-stage suprapubic prostatectomy the control of hæmorrhage tends to fall somewhat short of what is usually considered satisfactory in other operations. In the modern single-stage suprapubic prostatectomy, wide opening of the bladder neck will enable better hæmostasis, but even so in many cases there is difficulty in definitive control.

In retropubic prostatectomy the prostatic arteries can often be seen and suture-ligature can be applied; the control of bleeding is more satisfactory and secure than in other prostatic operations. Minor venous oozing from the capsule is not a factor of importance and is of almost no significance if continuous irrigation is used with retropubic prostatectomy. Our experience with 400 retropubic operations is that

\*Read by J.M.C. as a contribution to a symposium on prostatic surgery at the Montreal meeting of the American College of Surgeons, 1954.



primary and secondary hæmorrhage is less than with any other method.

2. *Incontinence.*—We are not going to suggest that incontinence is an important complication in transurethral resection in the hands of an experienced surgeon. However, it can occur, and in the hands of the less experienced it does occur. In suprapubic surgery it can occur also, although not very frequently. However, with less exact methods of hæmostasis, when a bag-catheter is used with traction, incontinence occasionally develops, and even though not complete is a very serious complication. Cases of this type also occur with long-standing stress incontinence.

In retropubic prostatectomy it is almost impossible to bring about incontinence. The apex is close to the fingertip, the isolation of the apical area is more exact, and scissors separation can be done without undue tension. For the experienced surgeon, this matter of incontinence is not a deciding issue, but for many it should be a factor to consider seriously.

3. *Stricture.*—Urethral trauma is most marked in transurethral resection. The cause is manipulation of a large sheath for up to an hour in an attempt to deal with a large gland. This has been admitted by most resectionists and is implied in the emphasis on perineal urethrostomy and on small calibre sheaths. Stricture remains an important complication in resection.

4. *Osteitis pubis.*—Osteitis pubis has been seen very rarely in prostatic operations. However, it has been encountered more commonly since retropubic prostatectomy has become popular. We have not seen a case. Great care must be taken throughout the operation to avoid trauma to the pubis, and excessive retraction and tension on the recti muscles must be avoided. In addition, we feel that maintenance of urethral drainage for a longer period decreases the tendency to extraprostatic collection of infected urine. Because of this, the catheter is left in position for five to eight days, and in addition the pre-vesical Penrose drain is not removed early; it is left in position for about one week, thus making sure that a small sinus leads down to the area of the wound in the capsule. These modifications may have some bearing on the absence of osteitis pubis.

We deal with all large prostatic adenomas by retropubic prostatectomy. For a long time it has been accepted without challenge that the ade-

noma must be approached according to its position in regard to capsule, bladder and rectum. However, there is little support for the rule along the lines of general surgery. The blood supply is at the bladder neck and below it, and we have found that the adenoma can be enucleated with ease if it is intravesical, or very prominent rectally. These cases can be operated upon by retropubic methods, and hæmostasis can be carefully established.

#### *Answering the patient's questions.*

What are the patient's anxieties if he has any discernment as he approaches prostatic surgery? He would like to know:

1. What are my chances of survival?
2. Will I have a good result? Will I pass a good stream of urine without distress?
3. Can you do it all in one operation?
4. Will I have trouble with this condition again?

#### *1. The chances of survival.*

Low mortality was an important factor for a long time in the popularity of transurethral resection. However, with improved methods in open surgery the mortality rate now is equal to that of transurethral resection, and the latter now has no advantage over open surgery as regards mortality.

#### *2. The results.*

We suppose no supporter of transurethral resection would challenge the claim of open surgery in regard to this point. If the adenoma is removed in its entirety, as in open methods, postoperative results are usually good; because transurethral resections are usually not complete adenectomies, there is greater assurance of a good result by open methods.

#### *3. One operation.*

Elective two-stage suprapubic prostatectomy is a long procedure, and it involves two major operations. This in itself accounts for its diminishing place in prostatic surgery. However, this does not imply that it is not a useful operation, and an essential one in a limited number of cases—the patient with poor kidney function, not responding to urethral drainage, the patient with a large stone and septic bladder, the patient with a vesical diverticulum which should be excised as a first-stage procedure in a poor-risk patient, and the patient requiring bladder drainage who cannot tolerate a urethral catheter.

Cases of this type are dealt with in two stages, and secondary suprapubic enucleation is usually the best method for removal of the adenoma. In some cases a secondary retropubic prostatectomy can be done. However, we have not developed much enthusiasm for this procedure and have used it in only three cases. It seems better to go ahead and do the enucleation through the sinus which is already established. Two-stage operation in transurethral resection is, of course, essential as a planned procedure if the surgeon aims at complete adenectomy in dealing with large glands. To ignore the necessity for planned two-stage resection simply means that a varying amount of tissue is left behind. No patient likes two major operations and this lends support to a single-stage suprapubic and retropubic prostatectomy as a method of choice.

#### 4. Recurrence of symptoms.

Anyone with considerable experience in transurethral resection realizes that this operation is frequently not a total adenectomy, even in the hands of very experienced men; with the large majority of resectionists it almost never is. It follows, therefore, that a certain percentage of patients develop recurrent obstruction in from one to ten years after the first operation. Now, we all know that in rare cases men have been operated on two and three times for complete removal of newly formed adenomata, but the development of new adenomata is really quite uncommon. One has merely to ask senior surgeons who have done open operations all their lives how many of these cases they have seen. This is not the explanation of recurrent obstruction in transurethral resection. The obstruction is not due to a new adenoma, but to recurrent growth in the remnants of the incompletely removed old adenoma. Evidence of this can usually be seen cystoscopically when recurrent obstruction develops. Because of this fact, in open surgery with complete adenectomy, the patient can be told that in all likelihood he will not have recurrent obstruction, whereas in transurethral resection the reply has to be more guarded.

#### SUMMARY

For most cases of prostatic hypertrophy, our operation of choice is retropubic prostatectomy. It provides a complete adenectomy with direct access and inspection of the prostatic capsule

and as low a mortality rate as in transurethral resection. There is less danger from primary and secondary hæmorrhage, and incontinence is extremely rare. There is an early dry wound and the postoperative results are good. Median bar and minimal hypertrophy are best dealt with by transurethral resection if the urethra is of adequate calibre. Single-stage and two-stage suprapubic prostatectomy are used occasionally. These two methods are indicated either when a poor-risk patient has poor kidney function or when there is an additional lesion in the bladder.

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#### EFFECTS OF DIGITOXIN UPON THE TWELVE LEAD ELECTROCARDIOGRAM

The effects of digitoxin upon standard 12 lead electrocardiogram recorded for 91 subjects have been analyzed by Broome, Estes and Orgain (*Am. J. Med.*, 21: 237, 1956). Tabulations and comparisons were made of the P-R intervals, the corrected Q-T intervals, the magnitudes of the S-T and T vectors, the individual lead S-T and T changes, and the frontal and spatial QRS-T angles.

The changes produced by digitoxin are: (1) mild lengthening of the P-R intervals; (2) usually distinct shortening of the Q-T interval so that, regardless of type of electrocardiographic abnormality, the Q-T intervals are all brought within the same range as the normals; (3) widening of the QRS-T angles, more readily detected in the abnormal; (4) increase in the magnitude of the S-T vector, especially prominent in those tracings in which electrical activity of the left ventricle is preponderant, such as left ventricular strain and left bundle branch block; (5) change in the S-T segment in a direction opposite to the major QRS deflection; (6) decrease in the magnitude of the T vector, especially in normal tracings; (7) change in the T wave in a direction opposite to the major QRS deflection.

Other well-recognized effects of the digitalis glycosides are straightening of the slope of the S-T segment from its origin to the region where it merges with the T wave, and relatively vertical slope of the T wave from its peak to the iso-electric line. These effects, along with the shortened Q-T interval and the ST-T changes generally opposite to the major QRS direction, are all consistent with the point of view that digitoxin acts to speed the repolarization process of ventricular muscle.

Since many of the electrocardiographic ST-T changes of ventricular strain and bundle branch block are similar to those of digitoxin effect, the latter are often not easily recognized in the presence of the former. Certain helpful changes may be present, however, particularly when two tracings are available for comparison. These are shorter Q-Tc interval, straighter slope of S-T segment, increased magnitude of the S-T vector and more vertical return of T from its peak to the iso-electric line. If the corrected Q-T interval is greater than 0.400 second, it is unlikely that digitoxin effect is present.

It has been pointed out that upon studying a single tracing in clinical practice, regardless of the general pattern, digitalis effect is difficult or impossible to detect in a surprising number of instances. Comparison of tracings made before and after digitalis administration demonstrates the drug effect far more clearly.



## Case Reports

### MUCORMYCOSIS OF THE CENTRAL NERVOUS SYSTEM

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D.T.M.&H., and  
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MUCORMYCOSIS of the central nervous system is a rare infection, of which only 13 case reports have been published hitherto.<sup>1-10</sup> It has been described as a complication of diabetes, acute

This is the second case of cerebral mucormycosis to be reported from Canada, and the youngest known to have occurred anywhere.

**History.**—The infant was born at her home in Hull, Que., on December 15, 1955, the birth weight being 6 lb. 4 oz. Details of the delivery and of development during the first week of life are not available, but on the seventh day the child became restless and cried frequently. Two days later she refused her feedings, and slight cough and sneezing developed. A physician was consulted, and admission to the Ottawa General Hospital was arranged on December 24, 1955.

**Physical examination.**—On admission the temperature was 94° F., the pulse rate 84 per minute, respiration rate 28 per minute. The infant was normally developed but markedly cyanotic and in severe dyspnoea. There was a "diaper rash" on the buttocks and vulva, and the umbilicus was slightly erythematous, with some brownish crusting. Examination of the chest showed

TABLE I.—SUMMARY OF CARDINAL CLINICAL AND PATHOLOGICAL FINDINGS IN 14 REPORTED CASES OF CEREBRAL MUCORMYCOSIS

Case No.	Reported by	Age and sex	Organs invaded	Concurrent disease	Vascular lesions	Orbital signs
1	Paltauf, 1885	Adult M.	Brain, lung, intestine	Intestinal ulceration	Not known	Not known
2	Gregory <i>et al.</i> , 1943	43 F.	Orbit, brain, meninges, pituitary, cavernous sinus, internal carotid	Diabetes	Thrombosis of left cavernous sinus, left internal carotid and circle of Willis	Severe. Left eye necrotic.
3	Gregory <i>et al.</i> , 1943	52 F.	Orbit, ethmoid air cells, brain	Diabetes	Thrombosis of orbital and cerebral vessels	Severe. Right eye enucleated
4	Gregory <i>et al.</i> , 1943	75 M.	Orbit, brain, meninges, spinal cord, pituitary	Diabetes	Invasion of meningeal veins	Severe. Proptosis of right eye. Bullous oedema and congestion of conjunctiva
5	LeCompte and Meissner, 1947	57 M.	Orbit, brain	Diabetes, haemochromatosis	Invasion of cerebral vessels	Severe. Right eye inflamed, swollen and purulent
6	Wolf and Cowen, 1949	42 M.	Brain, cavernous sinus	Diabetes	Thrombosis of cavernous sinus	Not described
7	Stratemeier, 1950	32 F.	Brain	Diabetes	Invasion of cerebral vessels	Left eyelid swollen and ptosed
8	Martin <i>et al.</i> , 1954	2½ mos. M.	Orbit, meninges, face, internal carotid, oesophagus, pleura, lungs, pancreas, bone marrow	Diarrhoea (antibiotics)	Thrombosis of left internal carotid	Severe. Left orbit necrotic
9	Kurrein, 1954	5 mos. M.	Brain	Acute nephritis and uraemia (antibiotics)	Invasion of cerebral vessels	None
10	Bauer <i>et al.</i> , 1955	40 M.	Orbit, nasal sinuses, brain, internal carotid	Diabetes	Thrombosis of right internal carotid	Complete right ophthalmoplegia
11	Bauer <i>et al.</i> , 1955	25 F.	Orbit, brain	Diabetes	Invasion of cerebral and meningeal vessels	Peri-orbital oedema, fixed pupil, retinal oedema
12	Gunson and Bowden, 1955	5 F.	Brain, internal carotid	Chronic glomerulonephritis	Thrombosis of left internal carotid	None
13	Baker, 1956	3 F.	Lungs, lymph nodes, nerves, orbit, internal carotid, brain	Diabetes	Thrombosis of left internal carotid, orbital and cerebral vessels	Left pupil larger than right. Haemorrhage in left eye
14	Present case	20 days F.	Brain, intestine	Congenital heart disease, pneumonia (antibiotics)	Invasion of cerebral vessels	Transient oedema of eyelids

and chronic intestinal inflammation, and acute and chronic glomerulonephritis (Table I). It is desired to record here a case in which the typical lesions were found at autopsy in a 20-day-old infant with congenital heart disease.

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diminished breath sounds on the right side with a prolonged expiratory phase. There was a systolic murmur over the left second and third interspaces in the parasternal line. The spleen was palpable 1.0 cm. below the costal margin.

**Laboratory data.**—The urine contained 1+ albumin and occasional erythrocytes, pus cells and epithelial cells. Unspecified yeast cells were also present. Chest radiography revealed normally aerated lungs and a globular heart with apparent enlargement of the left side. The appearance was suggestive of a congenital cardiac lesion.

**Treatment and progress.**—The infant was placed in an oxygen tent and was given nikethamide (Coramine), 1.0 ml. immediately, and Dicrysticin (penicillin and streptomycin), 1.0 ml. twice daily. The cyanosis improved somewhat, but on the following day respiration was gasping, and the temperature had risen to 99.6° F. Dicrysticin was supplemented by chloramphenicol, 0.25 ml. twice daily. By December 26, the child was breathing slowly and without effort, but the eyelids had become oedematous and the fontanelles appeared to be bulging. A lumbar puncture was performed. The cerebrospinal fluid was clear and colourless, and contained 150 white cells per c.mm., of which 97% were polymorphonuclear leukocytes and 3% lymphocytes. The sugar content was 81 mg. %. Direct smear revealed no organisms and culture was negative. The pressure and protein level were not recorded. Dyspnoea and cyanosis continued, and the temperature fluctuated between 98° and 99° F. The patient's condition deteriorated rapidly and death occurred early on January 4, 1956.

#### AUTOPSY REPORT

**Gross examination.**—The body was that of a poorly nourished, poorly developed white female infant weighing 2040 gm. and measuring 52.5 cm. in length. There was cyanosis of the skin and slight erythema and crusting of the umbilicus. The heart weighed 25 g. There was marked hypoplasia of the right ventricle. The walls of both ventricles measured 0.7 cm. in thickness. The pulmonic valve was almost completely stenosed, the orifice measuring 0.1 cm. in diameter. The foramen ovale and the ductus arteriosus were widely patent. The lungs weighed 15 g. each and were of normal appearance and consistency. The peritoneal cavity contained no free fluid. There was a perforation of the ileum, 25 cm. from the ileocaecal valve, measuring 0.5 x 1.0 cm., and having a slightly raised, firm, greyish edge. A layer of fibrinous exudate was present on the surrounding peritoneum. The brain weighed 340 g. On section there was a sharply demarcated hæmorrhagic area in the left temporal lobe, measuring 4 x 2 x 2 cm., extending to the cortex, and containing a ragged cavity in its centre, measuring approximately 0.6 cm. in its maximum diameter (Fig. 1). There was slight thickening of the overlying meninges. Smaller areas of similar appearance were seen in the white matter of both right and left frontal lobes. The largest of these areas measured 0.3 cm. in diameter. Other organs were unremarkable.

**Microscopic Examination.**—The lungs showed an infiltration of mononuclear cells into the alveolar walls, and similar cells were occasionally present within the alveolar spaces. Sections of the ileum included the margin of the perforation. The intestinal wall in this area showed evidence of necrosis and recent hæmorrhage, and was markedly thickened by a cellular infiltration composed almost exclusively of polymorphonuclear leukocytes. The submucosa in the region of the perforation was thickened and fibrosed, and the serosa was covered by a thick layer of fibrino-purulent exudate. The margins of the ulcer and the serosal exudate contained numerous thick-walled, branching, non-septate tubular structures, some of which were cut transversely and appeared as round or oval spaces (Fig. 2). These branching structures were morphologically similar to the hyphæ of fungi of the order Mucoraceæ. They were stained by both hæmatin and phloxine, showed up very clearly in periodic-acid-Schiff stained sections, in which they appeared a deep purple, and were Gram-positive. The right kidney showed a small ischæmic infarct in one of the papillæ. Step sections did not reveal the site of the vascular occlusion, and no fungi were seen. The left kidney was unremarkable. Sections of the brain revealed multiple areas of necrosis and patchy hæmor-



Fig. 1.—Cerebral mucormycosis; hæmorrhagic areas in brain.

rhage lying in the white matter and cortex. These contained numerous hyphæ, similar in appearance and staining characteristics to those described in the intestine (Fig. 3). The hyphæ were usually surrounded by polymorphonuclear leukocytes, but some were seen in neighbouring areas of apparently normal white matter without inflammatory reaction. They were occasionally intravascular in position. The meninges were thickened, and infiltrated by a mixed lymphocytic and polymorphonuclear exudate in which a few hyphæ were observed.

Sections of the thyroid, heart, liver, pancreas, adrenal and bone marrow were unremarkable.

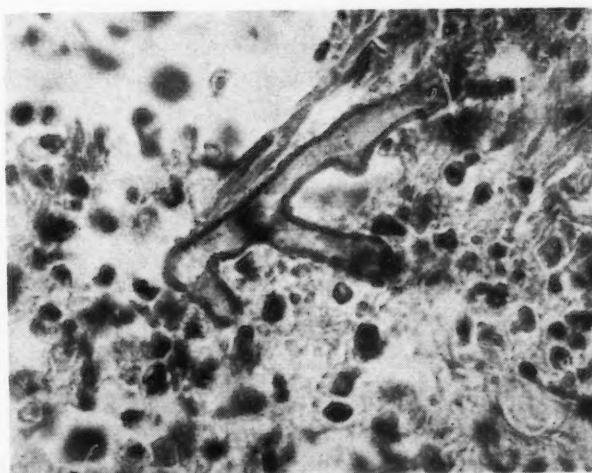


Fig. 2.—Cerebral mucormycosis; non-septate, branching hyphæ in wall of ileum. X 950.



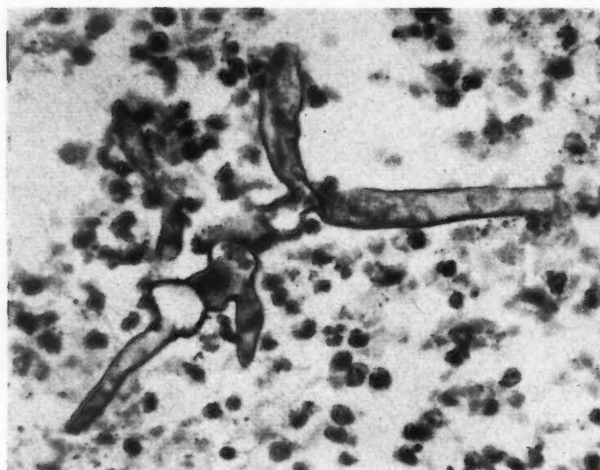


Fig. 3.—Cerebral mucormycosis; a section from the brain, showing inflammatory cells surrounding typical hyphae.  $\times 950$ .

#### COMMENT

The Mucoraceæ are primitive fungi of the class Phycomycetes, and owing to their ability to break down sugars are known as "sugar fungi". They are widespread saprophytes, and may be found as a cottony growth on dead or decaying animal or vegetable matter. The spores are wind-borne, and therefore may be inhaled. Parasitic infection of horses, cows, dogs, pigs and birds has been reported. In the human the organism is known to produce paronychia in orange pickers, and occasional cases of otomycosis.<sup>1</sup> Systemic infection is rare, the lungs being most frequently affected, as in the 16 cases collected by Baker.<sup>2</sup> Almost any organ may be invaded and in one instance the hyphae were found to be present in the subcutaneous tissues of the face, the eye and orbit, the brain, the œsophagus, pleuræ, lung, pancreas, and bone marrow.<sup>1</sup> Involvement of the central nervous system is infrequent, and has been reported only in patients with serious preceding disabilities. Thus cerebral mucormycosis has complicated diabetes (eight cases), hæmochromatosis, acute nephritis and uræmia, chronic glomerulonephritis and infantile diarrhoea. Five of the 14 cases have occurred in infancy or childhood. Salient points of the known cases are summarized in Table I.

The first case of cerebral mucormycosis was reported by Paltauf,<sup>3</sup> in 1885. Hafstrom, Sjoquist and Henschen published a second in 1941, but according to Kurrein,<sup>4</sup> neither the description nor the illustration warranted this diagnosis. Gregory, Golden and Haymaker<sup>5</sup> reported three cases in 1943. In 1947, LeCompte and

Meissner<sup>6</sup> reported a sixth, and Wolf and Cowen<sup>7</sup> reported one case in 1949. In the past six years, single instances of cerebral involvement have been observed by Baker,<sup>2</sup> Strate-meier,<sup>8</sup> Martin *et al.*,<sup>1</sup> and Kurrein.<sup>4</sup> Bauer *et al.*<sup>9</sup> reported two cases in 1955, and the first instance of the disease known to have occurred in Canada was described later in the same year by Gunson and Bowden.<sup>10</sup> In only one instance has the disease been diagnosed before death and the fungus identified conclusively by culture.<sup>9</sup> In four of the cases the paranasal sinuses have contained infected and necrotic material,<sup>5, 8, 9</sup> and on three occasions typical Mucor hyphae have been observed in this situation.<sup>5, 8, 9</sup> The fungus has invaded the orbit in eight cases and there have been well-marked clinical signs of orbital infection in nine (Table I). Invasion of blood vessels has been a constant feature, and hyphae have been observed in the cavernous sinus, internal carotid artery, and ophthalmic and cerebral vessels. Thrombosis usually follows. As stated above, the spores of the Mucoraceæ may be wind-borne and probably frequently gain access to the paranasal sinuses. This fact, together with the predilection of the organism for intravascular growth, and the frequency of orbital involvement, lends force to the suggestion of Gregory *et al.*<sup>5</sup> that the route of entry to the central nervous system may in some cases be from the paranasal sinuses via the angular vein, orbit, and ophthalmic veins. The sinuses were not examined at autopsy in the case reported here. There was no unequivocal clinical evidence of sinus or orbital infection and, although at one time œdema of the eyelids was noted, the portal of entry remains unknown. The middle ears were unremarkable.

It is a striking fact that in all but one of the adult cases the infection has complicated severe diabetes. This association was seen also in the case of a three-year-old child, but not in the infants, nor in the older child whose case was reported by Gunson and Bowden.<sup>10</sup> However, all but the latter received antibiotics, the possible role of which has been discussed briefly by Martin *et al.*<sup>1</sup> These authors quote Kligman<sup>11</sup> as suggesting that the destruction of a normal bacterial flora in a patient whose bodily defences are already lowered by serious disease may permit the multiplication and invasion of otherwise saprophytic fungi, an explanation which might well be applied to the case reported here.

# SUMMARY

A case of cerebral mucormycosis is described in a 20-day-old girl with congenital pulmonary stenosis, patent foramen ovale, and patent ductus arteriosus, who was receiving antibiotic therapy for pneumonia. This is believed to be the second case reported from Canada, and the youngest yet observed anywhere. The literature is reviewed briefly and the main features of each reported case summarized in table form. The remarkably frequent association of signs of orbital infection and meningo-encephalitis in adults with uncontrolled diabetes may render the diagnosis possible during life. This association is found in only one of the five cases occurring in infancy and childhood.

The authors wish to acknowledge their indebtedness to Dr. D. Magner, Professor of Pathology, University of Ottawa, for much helpful advice and criticism. The photomicrographs were made by Mr. R. Laframboise.

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## A TRUE CYST OF THE PANCREAS

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THE PANCREAS is prone to many kinds of disease, often with an unpleasant prognosis such as diabetes mellitus and carcinoma. Fortunately, there are rare cases which can benefit from proper surgical care by which the lesion can successfully be overcome. This is the case with pancreatic cysts.

Pancreatic cysts are not very common, and therefore, considering the few cases reported in the literature, we thought it worth while to publish a new case. Mousseau and Kling<sup>12</sup> have contributed an important study of pancreatic cysts with an extensive bibliography, so that we will only briefly survey the subject.

**Classification.**—Many authors have suggested classifications of pancreatic cysts. We prefer that of Bailey and Love,<sup>2</sup> with slight modifications.

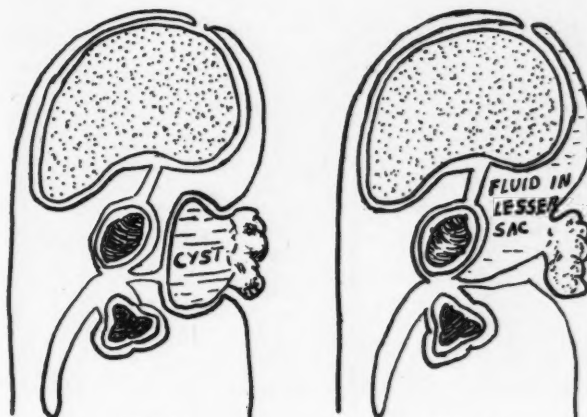


Fig. 1.—True pancreatic cyst. Fig. 2.—Pseudo-pancreatic cyst (after Bailey and Love<sup>2</sup>).

### True cysts (Fig. 1):

1. Retention cysts.
2. Cystadenoma.
3. Congenital cystic disease.
4. Hydatid cyst.
5. Degenerative or hæmorrhagic cysts (Robson and Cammidge<sup>15</sup>).
6. Dermoid cyst (Judd).

### Pseudocysts (Fig. 2).

By far the commoner are pseudocysts; of the true cysts, cystadenoma is the least infrequent.

**Symptoms.**—Pain of varying intensity, character and irradiation is almost always present; it has no specific characteristic. A history of trauma is rarely elicited.<sup>4</sup> Compression symptoms vary with the site of the cyst and the organs affected—stomach, colon, etc. A case of mediastinal pseudocyst has been reported in which the only complaint was of severe and progressive dyspnoea.<sup>8</sup>

**Signs.**—The most important sign is the clinical evidence of a palpable mass in the left upper quadrant. The tumour is of variable size and, if small, may not be palpable. Roentgenological study is very informative but not directly diagnostic.<sup>6</sup> A flat plate (Fig. 3) may visualize a soft tissue shadow. Barium examination may show various deformations due to extrinsic compression (Figs. 4 and 5). One cyst was revealed by aortography, the only symptom being subcostal pain.<sup>11</sup> Significant changes in pancreatic



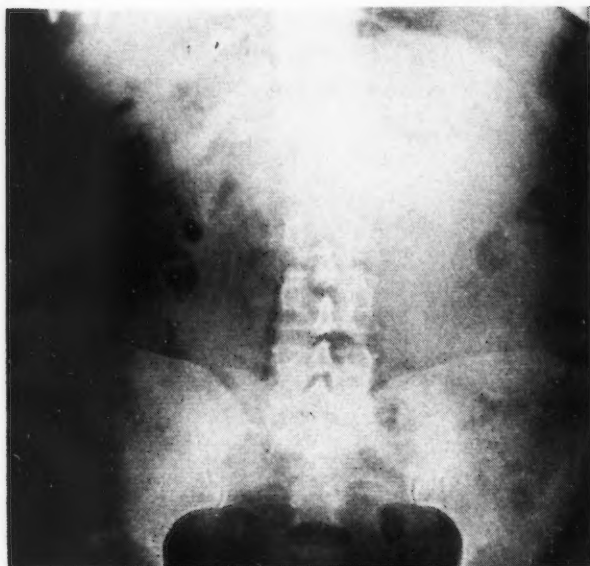


Fig. 3.—Flat plate of abdomen showing a large mass occupying left flank and upper quadrant. Intestinal gas surrounds the mass.

physiology may rarely be detectable by laboratory procedures.

**Diagnosis.**—"It is advisable to keep the possibility of a pancreatic cyst in mind in cases of upper abdominal complaints of rather obscure etiology," concluded Perl<sup>13</sup> in a case report on pancreatic pseudocyst. Differential diagnosis has to be made mainly from an ovarian cyst,<sup>2, 9, 17</sup> coeliac aneurysm,<sup>2</sup> retroperitoneal tumour, mesenteric cyst and renal tumour.<sup>1, 5</sup> Nevertheless the positive diagnosis is not infrequently made only after laparotomy.



Fig. 4.—The gastric fundus is compressed by an extrinsic mass.

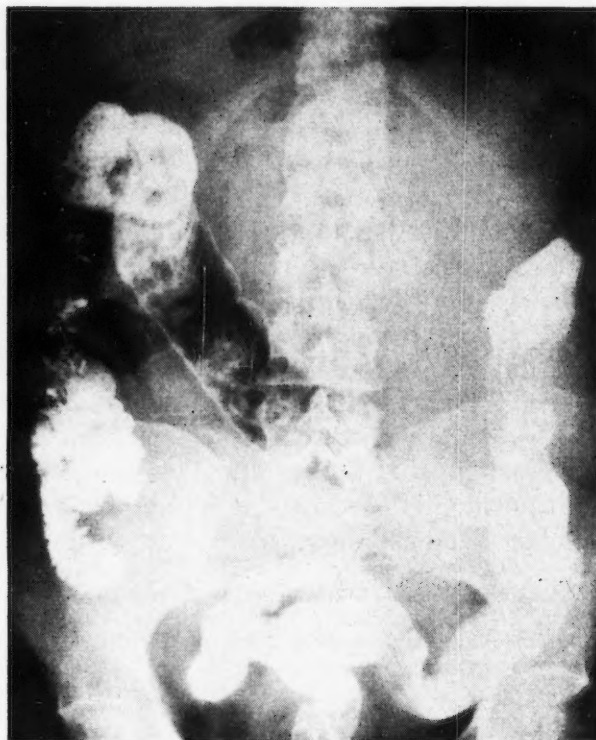


Fig. 5.—The transverse colon is pushed downwards by an extrinsic mass.

**Treatment.**—The treatment is exclusively surgical. Pseudocysts are preferably treated by marsupialization.<sup>2, 3, 14</sup> Anastomosis of the cyst to small intestine or stomach is rarely to be recommended,<sup>14</sup> but is considered by some as the treatment of choice for moderate and large benign cysts.<sup>10, 16</sup> Drainage of the cyst and section of the sphincter of Oddi has also been recommended for inflammatory pseudocyst.<sup>7</sup> Total excision may be risky because of the lack of true epithelial lining, but a successful case has been reported by Mousseau and Kling<sup>12</sup> without any sequel. Complete resection of true cysts is the best treatment and, when feasible, almost always affords a perfect recovery.

A white woman, Mrs. P.-E.G., aged 50, was seen at my office on February 18, 1953, complaining of a constant painful point in the left hypochondrium, dull in character, exacerbated by slight effort and by walking. Pain appeared after a fall on an icy surface one week previously, the trauma being directly to the left side of abdomen. She remembered having felt for three to four months a para-umbilical hardening, but she had never had any discomfort and never inquired about it. She did not complain of any gastro-intestinal upset, except mild intolerance to fats and chronic constipation of atonic type.

There was no gynaecological abnormality in the history, and she was still menstruating.

Physical examination revealed no clinical abnormality except that her blood pressure was 210/110 mm. Hg. In her abdomen was felt a large ovoid mass, about 6 inches in diameter, painful on palpation, mobile in all directions, not adherent to the skin or subcutaneous tissue, and extending from the midline of the abdomen

to the hypochondrium and flank. It was not palpable in the lumbar region.

Vaginal examination revealed a cystocele Grade I, faint softening of cervix and a bulging left fornix. The mass was thought, after bimanual examination, to be unrelated to the uterus or left adnexa.

The first diagnosis considered was that of an ovarian cyst with a very long pedicle. The possibility of a renal tumour was easily discarded, since it could not be palpated in the left lumbar region; so was coeliac aneurysm because there was no pulsation, thrill or murmur.

On admission to hospital, a barium enema eliminated the diagnosis of ovarian cyst, since the colon was displaced downwards. Barium meal revealed the relation to the stomach (Figs. 4 and 5).

Operation was performed on March 28, 1953. The surgeon found an enormous cyst of the tail of the pancreas, adherent to the splenic angle of colon and intricately related to the splenic vascular pedicle. Because of its relations with the surroundings, the cyst could not be removed intact; it burst before dissection could be completed. It was completely resected along with a part of the pancreatic tail, part of the transverse colon and the spleen.

*Pathological report.*—" . . . The lining of this cyst is formed by a thick layer of sclerosis covered at one point by muciparous cubic epithelium and containing a moderate chronic inflammatory infiltrate along with zones of lipophagic granuloma and cholesterol deposits (pancreatic cyst). . . ."—Carlton Auger, M.D.

#### CONCLUSIONS

Rather uncommon, true pancreatic cysts are of no surgical urgency. They should be removed because they lead to unpleasant symptoms and may sometimes burst or undergo transformation into a malignant tumour. Complete excision is the treatment of choice.

#### SUMMARY

A brief survey is given of pancreatic true cysts and pseudocysts. A case of true pancreatic cyst is reported with total removal; intestinal resection and splenectomy had to be performed because of definite compression lesions to transverse colon and spleen. Operation resulted in an uneventful immediate recovery. Unfortunately, we have heard that our patient died of

coronary occlusion about one year after the operation.

Acknowledgment must be made to Dr. Henri Lapointe, Professor of Radiology, Université Laval, Québec, Chief of the Department of Radiology, Hôpital de L'Enfant-Jésus, Québec, and to his staff for supplying me with roentgenological interpretations and photographs; to Dr. Carlton Auger, Professor of Pathology, Université Laval, Québec, and Chief Pathologist at the Hôpital de l'Enfant-Jésus, Québec, for the pathological report; and to my wife for her drawings.

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#### RÉSUMÉ

L'auteur rapporte un cas de kyste vrai du pancréas. Il profite de l'occasion pour exposer brièvement quelques généralités sur les kystes pancréatiques et sur leur traitement. Chez sa patiente, le seul symptôme fut une douleur, sous forme de point, dans l'hypochondre gauche survenue à la suite d'une chute. Les examens radiologiques ont beaucoup aidé à localiser la tumeur et à montrer ses rapports avec les organes voisins, mais le diagnostic définitif ne fut fait qu'à la salle d'opération. Il fut impossible de réséquer le kyste sans briser la capsule, mais il n'en fut pas moins enlevé au complet. Les lésions de voisinage ont nécessité une résection intestinale et une splénectomie. Nous avons appris que, un an après l'intervention, la patiente décédait d'une thrombose coronarienne. Les suites opératoires avaient été néanmoins absolument normales.

#### STUDENT SELECTION

"Allowing for exceptions to prove the rule, poor students, who are 'the despair of their teachers and the sorrow of their examiners,' rarely turn out to be excellent physicians. The initial selection of the medical student is probably the single most important factor in the making of a competent, wise, compassionate physician. It is surprising to me that no critical evaluation has been attempted of how we can improve our ability to select good candidates for medical schools. Much more careful thought must be given to this."—Walter Bauer, *Brit. M. J.*, 2: 1445, 1956.



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## BED REST FOR SICK CHILDREN?

Anyone who has struggled to confine an active child strictly to bed will appreciate that the exercise very frequently defeats its own object of securing rest. There are two questions with regard to bed rest in childhood: firstly, is it possible to enforce bed rest with the emphasis on "rest" in a given child; and, secondly, what are the benefits to be gained thereby?

Dr. John P. Gibson has recently given an interesting answer in a study of 1082 "feverish" children in office and private practice.<sup>1</sup> Hospital cases and more serious illnesses were specifically excluded.

Dr. Gibson's experience was that only 471 out of the 1082 feverish children would be likely to stay in bed for three days, based on the mothers' estimate. The mothers were therefore requested to keep these children in bed. As controls the remaining 611 were allowed up. The two groups were comparable in age, sex, type of illness, degree of fever and medication. Respiratory tract illnesses predominated in both groups (about 80%).

Four-fifths of the children in each group were afebrile by the fourth day and nearly all of them by the sixth day. Of the 20.4% who were still pyrexial in each group on the fourth day, two in each group developed otitis media. These were the only complications observed.

The results show that bed rest is of no value in favouring a return of temperature to normal in the "ordinary" or "self-limited" illnesses of children treated in the office or home. Neither was there apparently any likelihood of pre-

disposing to complications by allowing activity. Dr. Gibson's answer therefore is that rest is impossible to enforce in more than half of any group of children; and that no benefit accrues to children confined to bed. Dr. Gibson does not state in detail how much "rest" was obtained for his bed patients.

It was made clear that cases of serious illness such as rheumatic fever, typhoid fever or endocarditis were excluded. Cases in hospital were not studied, but the problem of bed rest also arises there. Dr. Gibson rightly remarks that advice must be suited to the individual and the circumstances, and this is even more true in hospital than outside. A bronchiectatic child is more likely to have pooling of secretions when in bed and develop pneumonia than when romping and coughing in the playroom, while the child who has rheumatic carditis should obviously be strictly in bed. However, the stage at which this same child with recovering carditis should be allowed up is rather more debatable.

Fortunately the penalties of recumbency in bed so common among adults and older people are relatively rare in children, but it is well to retain a critical faculty and re-examine, and possibly revise, from time to time, some conditions where therapeutic rest has tended to become hallowed by tradition.

This revision process has for example produced a much greater emphasis on exercise and early functional return in orthopaedics. A relatively common orthopaedic condition in childhood, osteochondritis dissecans of the hip (Legge-Calvé-Perthes disease), which formerly was treated by immobilization in bed for two to three years or more, is now treated in many centres by walking calipers. Bed rest is traditionally enjoined in childhood tuberculosis, and was at one time virtually the only treatment. It is certain that modern management, new drugs and surgery have very much reduced the length of rest necessary in some complicated cases. Anyone who has had much experience of young children during a long stay in hospital will probably have private doubts as to how much real bed "rest" is achieved, and may believe that the skilled supervision, adequate nutrition and steady routine in the hospital environment are the important benefits.

Gibson remarks that the higher the temperature the more willing was the child to remain in bed. This observation surely provides the clue as to what should guide our conduct of therapeutic rest. This guide, at least in acute illness, is the patient's inclination. Nature will enjoin rest when it is in the organism's best interest, either by malaise or pain or both. When these compelling factors are absent, it is surely officious, and often downright harmful to soma and psyche, to impose bed rest except under very special circumstances.

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## Editorial Comments

### CHRONIC DIARRHOEA

Acute diarrhoea usually presents no difficult problem of diagnosis or treatment; extensive investigation is rarely necessary and symptomatic treatment may be begun promptly and with good hopes of improvement. This happy situation does not pertain in chronic diarrhoea, where time-consuming clinical and laboratory investigations may be necessary before any rational treatment may hopefully be started.

The word diarrhoea means many things to many patients and it is well to restrict its use to the passage of frequent unformed stools. It may lead to the loss in the stools of up to 200 mEq. of sodium and 2,000 c.c. of water daily as compared to normal daily losses of 5 mEq. and 200 c.c. respectively. Attempts have been made to distinguish between large-stool diarrhoea (due to lesions of the small intestine and proximal colon) and small-stool diarrhoea (due to lesions of the distal colon)<sup>1</sup> but this concept does not seem to have gained widespread acceptance. Cooke<sup>2</sup> has classified chronic diarrhoea as due to systemic illness or lesions of the stomach, small intestine or colon, but emphasizes that the symptom depends finally on the condition of the colon itself, since severe derangements of small bowel and stomach function may be seen in the absence of diarrhoea. There is evidence that the colon is normally responsible for the daily reabsorption of up to 2,000 c.c. of water and isotonic amounts of sodium which are delivered to it by the small bowel. Interference with this remarkable process of reabsorption may result from disease of the wall of the colon, arrival in the colon of irritating

fluids or changes in colonic tone due to stimuli from the central nervous system.

Systemic causes of diarrhoea include Addison's disease, pernicious anaemia, diabetes mellitus, thyrotoxicosis and uraemia. Diarrhoea is not the usual presenting symptom in any of these diseases and they are usually recognized on other findings.

Diarrhoea of gastric origin is said by Capper<sup>3</sup> to occur very soon after meals and in the early hours of the morning; the stools are not usually watery and do not contain pus, blood or mucus. It may or may not be associated with surgical operations on the stomach. In the former group it is notable that diarrhoea due to achlorhydria is now considered to be very rare or non-existent; more common causes are alcoholic gastritis or the ingestion of irritating or coarse foods. Three out of nine patients had diarrhoea following total gastrectomy in one series cited by the same author. After partial gastrectomy diarrhoea may begin when the patient starts eating and subside without special treatment, or it may appear as a severe and sometimes fatal entero-colitis which appears on about the second postoperative day and is accompanied by severe shock. Mild diarrhoea may begin after the operation and persist with the loss of excess fat in the stools. This appears to be more common after the Polya operation than the Billroth I. Glazebrook and Welbourn<sup>4</sup> have demonstrated rapid transit of barium through the intestine and excessive peristaltic activity in such cases. Gastro-intestinal hurry is not always present, however, and some cases show marked torpor or spasm with slowing of the passage of barium.<sup>5</sup>

Diseases of the small and large bowel causing diarrhoea include chronic ulcerative colitis, carcinoma of the colon and rectum, diverticulitis, amebiasis, regional enteritis, idiopathic steatorrhoea and fistulae between various segments of bowel. A relatively new member of this group is the diarrhoea which follows the use of antibiotics. It may take the form of acute pseudomembranous entero-colitis, often seen in postoperative patients and associated with the presence in the stools of an antibiotic-resistant staphylococcus. More commonly a mild chronic diarrhoea may occur. Almy<sup>1</sup> describes hyperaemia of the rectal and sigmoid mucosa in such cases with the formation of a whitish, dry exudate. Recovery is often associated with the return of the faecal flora to normal after cessation of the antibiotics, and treatment consists of maintaining fluid balance until this occurs.

Steatorrhoea which consists of the passage of bulky, pale, greasy stools containing excessive amounts of fat, may be due to lesions of the pancreas (so that pancreatic lipase does not reach the bowel) or to failure of absorption of fat and other materials due to a defect of the small intestine. Pancreatogenous steatorrhoea



may follow chronic pancreatitis, carcinoma of the pancreas, pancreatectomy, or congenital cystic disease of the pancreas. Defects of the small intestine may be functional (idiopathic steatorrhœa) or due to regional enteritis, lymphosarcoma, resection of large segments of small bowel, gastro-jejuno-colic fistula, etc.

Emotional reactions to human problems are a commonly encountered cause of diarrhœa. When the diarrhœa is intermittent and clearly associated with emotional upsets, one may make the diagnosis on the basis of physical examination and history alone, but when the diarrhœa is chronic the diagnosis should be made only after a most careful examination of the gastrointestinal tract, as it is well recognized that psychoneurosis and organic disease may co-exist. Spurious diarrhœa due to fœcal impaction is common in elderly patients who are obliged to rest in bed. The diagnosis is often delayed through failure to perform a rectal examination.

In the investigation of chronic diarrhœa simple inspection of the stools is often of value and should not be left entirely to the nursing staff. The bulky, greasy, pale stool of steatorrhœa and the bloody, slimy stool of chronic ulcerative colitis may be recognized at a glance, although mere inspection is of course not diagnostic. Silvery stools have been reported in carcinoma of the ampulla of Vater, a lesion which may produce melœna and steatorrhœa simultaneously, but they have also been seen in steatorrhœa due to other causes.

Microscopic examination may reveal the presence of pus cells, red cells, parasites (*Giardia lamblia* or *Endamoeba histolytica*), fat globules or fatty acid crystals and undigested meat fibres. This examination may be conveniently done on a specimen obtained from the initial digital rectal examination or further specimens may be obtained from aspiration of suspicious-looking lesions during sigmoidoscopy. The finding of muscle fibres in a stool that has stood 24 hours is said to indicate pancreatic insufficiency; otherwise they may be found in a fresh stool or in any chronic diarrhœa.<sup>2</sup>

Fatty acid crystals are commonly increased in steatorrhœa but their absence does not exclude the diagnosis. *Giardia lamblia* is usually regarded as non-pathogenic but some patients excreting it are said to improve following the use of atabrine (mepacrine).

Past difficulties in interpreting chemical analyses of fœces have been largely overcome, according to Cooke,<sup>2</sup> through the observation that a person eating a diet of average fat content rarely excretes more than six grams of fat per day in the stools. If several repeated daily estimations show a loss greater than this, steatorrhœa or small bowel dysfunction is present. Determination of the percentage fat in random

stool specimens, the determination of split and unsplit fat and fat balance studies are rarely necessary. A rise in fœcal nitrogen (over two grams a day) is not now considered evidence of pancreatic dysfunction as it may occur in any chronic diarrhœa. In steatorrhœa fœcal nitrogen rises with fœcal fat regardless of the type of lesion underlying the steatorrhœa. The oral glucose tolerance test, which is often "flat" in steatorrhœa, is considered by the same author to be of limited value since wide ranges of results are found in any one disorder.

Radiological examinations of the stomach, small bowel and colon are important procedures but are often vitiated through failure to inform the radiologist of the patient's history and abnormal physical and laboratory findings. Flocculation of the barium in the small bowel indicates the presence of excess mucus but is not pathognomonic of steatorrhœa. For studies of small bowel mucosal pattern an examination using non-flocculating barium is advisable.

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#### GASTRIC CANCER IN PERSONS WITH ACHLORHYDRIA AND WITH PERNICIOUS ANÆMIA: A LESSON IN LOGIC

"Accordingly, it seems not unreasonable to accept the presumptive conclusion that in persons with low gastric acidity or pernicious anæmia the probability of occurrence of gastric cancer is greater than in persons with normal acidity."<sup>1</sup> In these words Berkson, Comfort and Butt<sup>1</sup> of the Mayo Clinic conclude a study of the incidence of gastric cancer in 1058 persons in whom low gastric acidity or pernicious anæmia had been recognized within the previous 15 years. As the authors indicate, this conclusion differs in no way from what has been generally accepted for many years. Thus the reader who reads only conclusions will gain only some slight support for his impression. But he who carefully reads the whole report, who goes over with the authors the simple arithmetic entirely free from statistical jargon, reasons with them in a straight line, takes note with them of the inconsistencies and incongruities that challenge otherwise seemingly sound assumptions and de-

ductions — this reader will enjoy with the authors "the real labour of thought". He will admire the lucidity with which they state the case, present previous findings, check them and qualify the conclusions with larger data. He will be fascinated in seeing how they set up straw men, seemingly prop them up with both logic and figures and then, with a word of common sense, knock them down and obliterate them. He will never again take the vital statistics of mortality from gastric cancer or from cancer of any other internal site, or for that matter, of any site at their face value. He will demand that, before any deductions are drawn from such data and even before the data are presented for general consumption, their quality will be established by comparison and reason. And he will fully realize that changes in recorded mortality rates from cancers of any specific site should be attributed to artifact until proven otherwise. He will thank Berkson *et al.* for their clear demonstration that the whole truth is not easily come by. He will see, too, in this report, the potentialities for investigation that lie in all hospital data now so often buried in dust-collecting histories.

N.E.M.

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#### DEXTRAN SULFATE AS A SUBSTITUTE FOR HEPARIN

Many attempts have been made to find a suitable substitute for the anticoagulant heparin. In spite of the fact that it occurs naturally, heparin is difficult and expensive to prepare. It belongs to a large group of substances chemically classified as sulfated polysaccharides. These compounds abound in nature and attempts have been made to prepare heparin substitutes from algæ<sup>1</sup> and molluscs.<sup>2</sup> Synthetic heparin substitutes have also been prepared by sulfation of polysaccharides. Clinical trials have been carried out on Paritol (alginic acid sulfate), Thrombocid (xylan sulfate) and Dexulate (dextran sulfate).

Dextran sulfate, prepared from the plasma expander dextran, appears to be the most promising of these substances. Early trials with dextran sulfate of high molecular weight showed severe side-reactions with destruction of fibrinogen and clumping of platelets. If the molecular weight was about 7,500, these effects did not occur.

When dextran sulfate was injected intravenously into humans, it differed from heparin.<sup>3,4</sup> A single dose of dextran sulfate produced

an anticoagulant effect lasting approximately twice as long as did a comparable dose of heparin. A second important difference was the accumulation of dextran sulfate that occurred after three to five days with repeated injections. This allowed a reduction both in the size of the dose and the frequency of administration. The cumulative effect was explained by the slow destruction of dextran sulfate in the body and the gradual filling of the extravascular compartment. It should be pointed out that the unit of dextran sulfate quoted by Jeavons is four times as heavy as the unit of heparin, and the total sulfur content is six times as great. On this basis it is not surprising that the body takes longer to metabolize dextran sulfate than heparin.

There has been no satisfactory answer to what will happen to accumulated dextran sulfate when protamine sulfate is injected intravenously as an antidote for bleeding. It is well known that protamine sulfate has a transient effect limited to the heparin in the blood stream.<sup>5</sup>

The cumulative effect was regarded by Jeavons and co-workers as an advantage over heparin in the maintenance of anticoagulant therapy. Serious bleeding was not encountered in the small number of cases treated. With more experience the cumulative effect may prove dangerous. Heparin caused significantly more bleeding than the oral anticoagulants,<sup>6</sup> and it is unlikely that dextran sulfate will differ greatly from heparin in this respect.

An interesting effect of dextran sulfate was the appearance of alopecia in approximately 10% of patients. This has been reported with other sulfuric esters of polysaccharides. No explanation has been advanced. Diarrhoea with blood in the stools occurred in two of the 11 patients treated. Dextran sulfate caused clearing of alimentary lipæmia. At first the level of serum cholesterol fell, but after three to five days when the dose of dextran sulfate was reduced because of the cumulative effect the fall was not maintained. To cause continued lowering of serum cholesterol a dose of dextran sulfate would be required that would result in a dangerous prolongation of the clotting time.

Dextran sulfate is a very interesting compound, but its advantages over heparin await further observations.

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## Medical News in brief

### HAZARDS IN THE TREATMENT OF ACUTE MYOCARDIAL INFARCTION

In spite of major advances in diagnosis and therapy, it must still be recognized that, under proper supervision, a large proportion of patients with myocardial infarction will run their course from beginning to end with little or no need for medication. Russek (*Am. J. M. Sc.*, 232: 403, 1956) suggests that over-treatment, arising from the application of "routine" programs, may be the cause of disability and death in some cases, and should be discouraged. He indicates that, by adherence to the important principle of treating each patient individually, the dangers of indiscriminate therapy may be avoided; and he stresses that the use of potentially dangerous agents in acute coronary occlusion *without clear indication* is not justified.

In this paper are listed and discussed drugs and procedures sometimes "routinely" used in certain centres; their disadvantages and deleterious effects, when improperly or unnecessarily used, are described.

These drugs and procedures include: administration of nitroglycerin, morphine, oxygen, anticoagulants, digitalis, quinidine, procaine amide, pressor agents, aminophylline, papaverine, and alcohol, and even bed rest, "chair" treatment and hospitalization. All these drugs or methods, although individually and collectively having an important place in the treatment of acute myocardial infarction, may still be harmful in individual cases, when unnecessarily or improperly used.

### THE THYROID PROFILE

A review of thyroid function studies was undertaken by Perloff (*Am. J. M. Sc.*, 232: 443, 1956) to clarify some of the erroneous conceptions prevalent among practising physicians. In certain cases, a complete investigation of thyroid function may be the only method of clarifying an obscure diagnostic problem. Determinations of radioactive iodine uptake by the thyroid gland, the serum conversion ratio, and the serum levels of protein-bound iodine are usually the most helpful tests of thyroid function. However, it must be admitted that the wise clinician, who refuses to allow himself to be stampeded into a precipitate therapeutic decision, may in many cases establish the correct diagnosis without using any of these complicated and expensive procedures. A therapeutic trial with thyroid extract in alternation with a placebo can sometimes serve to differentiate patients with hypothyroidism from individuals with fatigue and inertia from other causes. Generally speaking, the diagnosis of hyperthyroidism is often clear when the patient presents himself for the first consultation. If the hyperthyroidism is so mild that the physician cannot determine whether or not his patient is truly thyrotoxic, he should perhaps wait until the metabolic

disorder becomes more obvious since, under such conditions, the hyperthyroidism does not represent an immediate danger to the patient, provided that it is not associated with cardiac insufficiency, tuberculosis, or diabetes. If he initiates treatment, for example with thiouracil, the physician finds himself confronted with the need for a long therapeutic course. For this reason, it is strongly recommended that a definitive diagnosis be established before therapy is initiated. This should be done clinically if possible but, if this is impossible, it may be carried out by one or more of the thyroid function studies in general usage.

### INTRAPARTUM INFECTION AND PERINATAL DEATH

A trial is reported from Manchester, England, (*Lancet*, 2: 903, 1956) of treatment of fetal infection as a major cause of perinatal death. Two groups of women either in labour or with ruptured membranes were selected on admission: (1) those thought to have an intrapartum infection and treated alternately by antibiotics or without antibiotics; (2) controls in whom no intrapartum infection was suspected. Diagnosis of fetal infection was based on two criteria which were later found to be reliable: (1) maternal pyrexia; (2) fetal tachycardia with a rate of 160 or more sustained for at least ten minutes. Full bacteriological examinations were made in all cases, including use of vaginal swabs, catheter specimens of urine, fetal blood specimens and autopsy specimens where the fetus was stillborn or died later.

Intrapartum pyrexia was found to be associated with an increased incidence of pathogens in the genital tract. Pneumonia in the fetus was commonly associated with evidence of intrapartum infection lasting for more than 48 hours in the mother. Perinatal death in cases of infection was shown to be significantly reduced in incidence if it was possible to treat the mother for at least 48 hours before delivery with a combination of intramuscular streptomycin 1 g. twice daily and oxytetracycline 500 mg. by mouth six-hourly.

### LOCAL HYDROCORTISONE IN ULCERATIVE COLITIS

A group of patients with ulcerative colitis in a mild or moderate stage were treated by rectal introduction of a hydrocortisone solution by slow drip. The solution contained 250 mg. of hydrocortisone dissolved in 50 c.c. of 50% ethyl alcohol and diluted down with 500 c.c. of normal saline. The treatment was given nightly, for two to three weeks; 21 courses of treatment have been given to 17 patients. In 14 instances there was rapid clinical remission within a few days of starting treatment. In one case the patient was improved and in six cases treatment was without effect. The sigmoidoscopic picture also improved, but histological findings did not. This treatment is of temporary benefit; repeated courses may prove effective in dealing with recurrence of symptoms.—Truelove, *Brit. M. J.*, 2: 1267, 1956.

(Continued on advertising page 47)

## REVIEW ARTICLE

### CITRATE INTOXICATION\*

EDMUND R. YENDT, *Toronto*

DURING THE PAST few years there has been increasing concern over the danger of citrate intoxication resulting from multiple transfusions of citrated blood.<sup>1,2</sup> It is the purpose of this paper to discuss the normal metabolism of citric acid and to review the literature on citrate intoxication.

Citric acid is widely distributed in human tissues and fluids, but by far the highest concentration is in the bones.<sup>3</sup> It has been estimated that over 95% of the total citric acid of the body resides in the skeleton.<sup>4</sup> Although the significance of the tremendous concentration of citrate in bone is as yet uncertain, present information on the interrelationship of calcium and citrate metabolism suggests that it may be one of considerable importance. Citric acid combines with calcium to form a diffusible but poorly ionized complex.<sup>5,6</sup> Much of the calcium bound to citrate is thus rendered biologically inactive, at least as far as its role in the function of cardiac muscle, skeletal muscle and blood clotting is concerned; calcium must be present in the ionized form to perform these functions. Normally, the concentration of citrate in human serum is quite low: between 2 and 3 milligrams per 100 millilitres, and the amount of calcium which is bound to it as a complex is quite insignificant: probably less than 0.5 mg. per 100 ml.<sup>6</sup>

Further relationships between citric acid and calcium metabolism have been demonstrated. It has been shown experimentally that injections of parathyroid extract are followed by rises in serum citrate levels and that, after parathyroidectomy, the concentration of citrate in the serum decreases.<sup>7,8</sup> However, comparable rises in citrate levels occur after intravenous injections of calcium salts.<sup>7</sup> Moreover, elevated serum citrate levels have been found in various other hypercalcaemic states such as hypervitaminosis D and metastatic carcinoma. It would appear therefore that serum citrate concentrations are in some way determined by the amount of calcium in the body fluids and that, when the concentration of calcium in the serum is increased, the serum citrate also rises, and vice versa. The changes in citrate levels occurring in the aforementioned conditions are not sufficiently great to be of clinical significance.

There is evidence which suggests that the administration of vitamin D has an influence on citrate metabolism which is primary rather than secondary to coincident changes in calcium

metabolism. In human and experimental rickets, serum citrate levels are low irrespective of calcium levels, and the administration of vitamin D to rachitic rats results in a prompt increase in citrate concentration which is not preceded by a change in calcium levels.<sup>9,11</sup>

The role of citric acid in the intermediary metabolism of carbohydrate, fat and protein has been more clearly defined. Citric acid is an important member of the Krebs tricarboxylic or citric acid cycle. This cycle forms the common metabolic pathway wherein the 2-carbon or acetate fragments derived from the breakdown of carbohydrate, fat and protein undergo final oxidation to carbon dioxide and water with the release of energy. This system has been demonstrated in many tissues but the most important sites probably are the liver and muscle. The remarkable ability of the healthy liver to metabolize citrate has been demonstrated in animal experiments in which livers were perfused with citrate. It was found that 100 times the normal concentration of citrate in blood could be cleared in one passage through the liver.<sup>12</sup> However, in hepatic dysfunction, an increase in resting values of serum citrate and slower removal of injected citrate have been observed.<sup>12</sup> In addition to its utilization by liver and muscle, citric acid is excreted and concentrated by the kidney.<sup>13</sup> The concentration of citric acid in the urine is normally 15 to 20 times that of serum.

Because of its rapid utilization under normal conditions, citrate has been regarded as a perfectly safe anticoagulant for blood and the danger of citric acid intoxication resulting from the transfusion of citrated blood has been thought to be negligible.<sup>14</sup> But there now appears to be good evidence that citrate concentrations may rise to toxic levels when large quantities of citrated blood are given rapidly.

Evidence of citrate intoxication occurring in humans was first presented by Wexler *et al.*<sup>15</sup> They found tremendous increases of serum citrate concentrations in erythroblastotic infants receiving exchange transfusions. In one case the serum citrate was 150 mg. per 100 ml., which is 50 times or more the concentration normally present in serum. Tetany has occurred in some infants<sup>15,16</sup> and deaths have been reported.<sup>15-17</sup>

During exchange transfusions in infants blood is given very rapidly, 500 ml. usually being administered in one hour. This results in citrate being infused at a rate of approximately 5 to 10 mg. per kg. of bodyweight per minute. Such rapid rates of citrate administration are unlikely to occur in adults. Studies which are applicable to conditions in adults have been reported by Bunker and his associates.<sup>18</sup> Serum citrate levels were determined in 130 patients who were transfused with varying amounts of citrated blood. There was no serious accumulation of citrate when the rate

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of transfusion in adults without liver disease did not exceed 500 ml. every 30 minutes. However, when the rate was doubled to 500 ml. every 15 minutes, about one-half of the patients without liver disease and all those with liver disease had serum citrate levels above 9 mg. per 100 ml. Serum citrate concentrations above this level are apt to result in significant reduction of the amount of *ionized* calcium in the extracellular fluids. It is unlikely, however, that levels of *ionized* calcium are seriously reduced by citrate concentrations of less than 25 mg. %. In this series of 130 cases, there were seven patients who had citrate concentrations greater than 25 mg. per 100 ml. The calculated rate of infusion of citrate in these seven cases was usually 1.0 mg. per kg. of bodyweight per minute, or more. Although the authors report that it was usually necessary to give blood at the rate of 500 ml. every 15 minutes before such a rate of citrate infusion occurred, these figures are not necessarily applicable when blood is obtained from the banks of many Canadian hospitals and from the Canadian Red Cross. Blood obtained from these sources may have a higher citrate content than that supplied by the blood bank of the Massachusetts General Hospital, which was the source of some of the blood used in this study. When blood with higher citrate content is used, a dangerous rate of citrate infusion, namely 1.0 mg. per kg. of bodyweight per minute, may occur when 500 ml. are given every 30 minutes or faster.

Data obtained in the study of Bunker and associates also suggest that there is increased danger of citrate intoxication in hypothermia and during any cardiac or great vessel surgery which produces mechanical obstruction to the hepatic circulation.

As yet no direct toxic effect of the citrate ion has been demonstrated. The harmful results of citrate accumulation are presumably due to depression of *ionized* calcium levels. Hastings and his associates<sup>5</sup> have suggested a formula for the calculation of *ionized* calcium levels when values for the total concentrations of calcium and citrate are known. If one calculates the level of ionized calcium in the serum when the citrate concentration rises to 25 mg. per 100 ml., values of 2.2 mg. per 100 ml. or less may be obtained, the normal level being 4.0 to 5.0 mg. %. When the concentration of ionized calcium in the extracellular fluids is decreased to such a degree, tetany and impairment of cardiac function are apt to occur.

Tetany has been reported in children but was not observed in any of the patients studied by Bunker and his associates.<sup>18</sup> In the Toronto General Hospital tetany has been observed in one patient thought to have had citrate intoxication. The diagnosis was not proven because citrate determinations were not being performed at that time.

### CASE REPORT\*

The patient, a 29-year-old woman suffering from a severe delayed post-partum hæmorrhage, was admitted to hospital in profound shock. A dilatation and curettage was performed immediately but severe bleeding continued and shock persisted for at least four hours despite transfusions with large quantities of blood and dextran. Four hours after admission to hospital a hysterectomy was performed; in the lower uterine segment a tear was found, which was presumably the cause of the post-partum hæmorrhage. During the operation it was difficult to control the bleeding. In the postoperative period the systolic blood pressure was maintained at 100 mm. Hg until shortly before death but her Hb. level was never above 6.5 g. per 100 ml. Nine hours after the operation she suffered tetany, which responded to the intravenous administration of calcium gluconate. Later, hyperventilation occurred followed by decreasing levels of consciousness and finally convulsions; she died 32 hours after admission to hospital.

At autopsy there was marked cerebral cedema and evidence of widespread tissue anoxia.

During the first 16 hours in hospital this patient received eight litres of citrated blood. Most of the blood (six litres) was given during the first five hours and in this period the rate of citrate infusion was 1.36 mg. per kg. of bodyweight per minute—a rate likely to produce toxic citrate levels. The total serum calcium was normal, as is usually the case in citrate intoxication. The patient also had an unexplained metabolic acidosis which ruled out hyperventilation as a cause of her tetany. Her venous blood pH was 7.22; serum sodium, 136 mEq./l.; serum potassium, 4.2 mEq./l.; serum chlorides, 108 mEq./l.; and carbon dioxide combining power, 7.7 mEq./l. In the absence of hypocalcæmia and alkalosis it was concluded that the tetany was probably due to citrate intoxication. Whether citrate intoxication was a significant factor in causing death is uncertain.

The harmful effects of citrated blood on the action of cardiac muscle are a much more serious manifestation of citrate intoxication. These effects are a decreased force of systolic contraction with resultant hypotension and a tendency towards arrhythmias, especially ventricular fibrillation. The isolated frog heart preparation of McLean and Hastings<sup>19</sup> stops beating when the level of ionized calcium in the perfusing fluid falls to 2.0 mg. %. Clinically, hypotensive episodes have been encountered when citrate levels were excessively high even though blood replacement seemed adequate. Such hypotensive episodes have responded to the intravenous administration of calcium salts.<sup>18</sup>

The adverse effect of citrated blood on cardiac function has been demonstrated experimentally by Cookson *et al.*<sup>20</sup> in animals. They performed experiments on 22 dogs. In each dog, shock was produced by the rapid withdrawal of 45 to 50% of the calculated blood volume.

\*The author wishes to thank Professor D. E. Cannell of the Dept. of Obstetrics and Gynaecology for permission to report this case.

In one-half of the animals the blood was then replaced with heparinized blood. All these dogs showed immediate and complete recovery from shock. In the remaining animals, citrated blood was used for replacement. Only one of these dogs showed rapid and complete recovery. In the dogs that failed to respond, cardiac output was greatly reduced and the right atria were engorged. Depression of heart action was reversed in several experiments by an intracardiac injection of 3 to 5 ml. of 10% calcium chloride. These investigators also had the impression that hypothermic dogs were more susceptible to citrate intoxication. When such animals were transfused with citrated blood under the experimental conditions described above, the incidence of cardiac arrest was high.

Disturbances in blood coagulation have also been noted after multiple transfusions with citrated blood. It has been suggested that these hæmorrhagic complications might be due in part to the marked lowering of ionized calcium resulting from citrate accumulation. Stefanini<sup>21</sup> has reported a slight prolongation of clotting time when the *ionized* calcium level falls to 2.0 mg. %. However, factors other than lowering of ionized calcium levels are probably of much greater importance. Recent studies<sup>22, 23</sup> suggest that thrombocytopenia and diminished concentrations of prothrombin accelerator factors may be the responsible causes. Such an explanation seems reasonable because stored blood has a decreased titre of prothrombin accelerators, and platelets are almost non-existent.

The answers to certain problems concerning citrate intoxication cannot be found in the available literature on the subject. For instance, present information does not indicate how long serum citrate levels might remain elevated once the state of citrate intoxication has been established. If our patient referred to in this paper actually did suffer from citrate intoxication, there is a suggestion that high citrate levels may persist for several hours after the rate of transfusion is greatly reduced. During the first five hours in hospital this patient received six litres of blood but had no tetany. In the ensuing nine hours she received only an additional two litres of blood, given at widely spaced intervals, and yet at the end of this time tetany developed. Our patient also had a metabolic acidosis, the cause of which was not determined; there was no evidence of renal insufficiency, diabetes or ketosis. It is possible that this acidotic state could also have been due to citrate intoxication. Although trisodium citrate is the salt commonly used for anticoagulant purposes, the serum sodium does not become elevated despite marked rises in citrate levels.<sup>15</sup> Theoretically a high citrate concentration in the extracellular fluids, by increasing the anion content without any material alteration of the cations, should produce a metabolic acidosis. It is hoped that

future studies will clarify this aspect of the problem.

Treatment of established or incipient citrate intoxication is by intravenous injection of calcium salts. Attacks of tetany, depressed heart action and hypotensive episodes have all been reported to respond to such treatment. However, it is difficult to calculate the correct dose of calcium since *the total serum calcium usually remains within normal limits*. Determination of the level of *ionized* calcium in the serum would aid in the calculation of the proper dose but the only available method is a biological one utilizing the frog heart preparation of McLean and Hastings and it is not suitable for routine hospital purposes. Likewise, citrate determinations are difficult and cannot be done in most routine laboratories. Since the treatment of the condition is unsatisfactory, the avoidance of excessively large or rapid transfusions of citrated blood is advisable. This is especially desirable when factors such as liver disease, hypothermia or obstruction to the hepatic circulation increase the likelihood of citrate intoxication.

A suitable substitute for citrated blood is being sought. Oxygenated red cells suspended in Ringer-Locke gelatin solution,<sup>20</sup> red cells suspended in salt-free dextran<sup>24</sup> and blood from which calcium has been removed by passage over an ion exchange resin<sup>18</sup> have all been suggested as alternative materials for blood transfusions. The disadvantage of all these substitutes is the complicated method of their preparation.

#### SUMMARY

1. When citrate is injected at the rate of 1.0 mg. per kg. of bodyweight per minute, there is danger of its accumulation to toxic levels. Such a rate of citrate infusion occurs when blood from many hospital and Red Cross banks is transfused at the rate of 500 ml. every 30 minutes or faster.

2. The danger of citrate intoxication is greater in the presence of liver disease. In patients undergoing cardiac and great vessel surgery, mechanical obstruction to the hepatic circulation could have a similar effect. Induced hypothermia might also increase the danger since many metabolic processes, including the rate of citrate utilization, are apt to be depressed by lowered body temperatures.

3. The toxic effects of citrate are thought to result from decreased levels of ionized calcium in the extracellular fluids. Marked lowering of *ionized* calcium levels may result in tetany and impaired heart action. The latter may lead to hypotension despite adequate blood replacement and also to an increased danger of ventricular fibrillation and cardiac arrest.

4. The treatment of citrate intoxication is by the intravenous administration of calcium salts. However, such treatment is not completely satisfactory and there is need for an easily pre-



pared alternative to citrated blood for transfusion purposes. If possible, it is desirable to avoid the rapid transfusion of large amounts of citrated blood.

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## PUBLIC RELATIONS FORUM

Conducted by L. W. HOLMES  
Assistant Secretary, C.M.A.

PUBLIC ATTITUDES  
TOWARDS DOCTORS. V.

THERE WAS A TIME when the course of a public relations program was guided "by guess, by God and by intuition." Fortunately, the folly of such haphazard programming has been recognized by most practitioners. Today facts form the bedrock of the sound public relations program and on this foundation creative intelligence and imagination build.

One of the most effective fact-finding tools used in public relations is the public opinion survey. This type of research attempts to measure the extent and intensity of public attitudes and/or to determine the reasons for such attitudes.

The last four articles in this column reported some of the important findings of such a public opinion study conducted for the American Medical Association. Unfortunately, this particular survey answered only the question "How much?" not "Why?" However, armed with only this information one may attempt, albeit skating on

thin ice,\* to suggest reasons for some of the attitudes reported and to examine some of the implications of the findings.

## THE FAMILY DOCTOR

Perhaps the two most important facts revealed by the survey are:

1. People who have a family doctor hold more favourable attitudes towards the medical profession than those who have no doctor.

2. People hold their own doctor in greater esteem than they do doctors generally.

The first of these findings points up the importance of promoting the family doctor concept. The family doctor is frequently the individual's only contact with the medical profession. For many laymen, lacking contact with the profession, medicine and its practitioners have always been surrounded by an aura of myth, magic and mystery. People fear the unknown and probably dislike that which they fear.

The family doctor can do much to dispel this fear and to prove to his patients that the doctor is a likable human being, not an impersonal demi-god.

But to urge people to acquire a family physician is not enough. Some mechanism must be set up through which people may make a wise choice of doctor on the bases of propinquity, age, sex, religion, etc. It is encouraging to learn that the College of General Practice is actively studying this problem and is urging its provincial chapters to develop a program to meet this need. The British Columbia Division of the C.M.A., too, has offered its assistance to persons seeking a family doctor.

In addition to helping to improve public attitudes towards the medical profession, it is obvious that acquisition of a family doctor will do much to eliminate the public criticism that doctors are difficult to reach in an emergency. But more of this criticism later.

The revelation that people think much more highly of their own doctor than they do of doctors generally poses a most difficult public relations problem. The reason for this phenomenon is no doubt complex and consequently the solution will not be simple.

To the individual his family doctor is someone very special. The choice has probably been his own. Because of this ego involvement, to say that all doctors are as good as his own would be a reflection on his own judgment. But personal experience is also an important factor. The medical profession has acquired a stereotyped personality through publicity seen in the newspapers, magazines and on television, and heard on the radio and from neighbours. From experience the patient knows his own doctor as

\*A Toronto psychologist, Grant McMurray, Ph.D., is a "partner on skates". I should like to acknowledge his help in assessing the "public mind" as reflected in the survey results.

an individual and a human being—an exception to the general rule.

It would appear, too, that to criticize the medical profession is the accepted thing, and society today frowns on the nonconformist. Additionally, most of us have a tendency to exaggerate. The patient who is kept waiting for 15 minutes in a doctor's waiting room will stretch this wait to an hour in the telling, particularly if he is participating in a conversation highly critical of the medical profession.

#### IN THE DOCTOR'S OFFICE

In dealing with patients, doctors come in for considerable criticism on several counts:

1. They don't give patients as much time as the patient would like.
2. They aren't frank enough in telling patients about their illnesses.
3. They hide other doctors' mistakes.
4. They are difficult to reach in emergencies.
5. They don't have enough personal interest in the patient.
6. They charge too much and plan to get rich quick.
7. They have the idea they are always right.
8. They keep people with appointments waiting longer than necessary.
9. Their charges have gone up faster than other living costs.

It will be apparent to the reader that almost all of these criticisms can only be met by the doctor in his practice. All the public relations programs in the world cannot remove the doctor's responsibilities for paying attention to the improvement of doctor-patient relationships. Patients want personalized treatment. They want to feel that theirs is the most important case the doctor has. They want the doctor to be ego-satisfying and empathetic. Fortunately the doctor who can qualify!

The criticism that doctors are hard to reach in emergencies has already been mentioned in discussing the family doctor. The development of Emergency Call Systems across the country is doing much to solve this problem.

On the problem of waiting-room time perhaps an excerpt from an address by A.M.A. President Dwight H. Murray is worthy of note:

"Personally, I do not believe doctors have a monopoly on being busy. Everyone is busy. The business or professional man, the factory worker, the housewife, and even the retired person usually have a thousand and one things to do. The complexity of modern life forces everyone to be busy. I sincerely feel that we should make every effort to conserve the patient's time while he is in our reception room. Many complaints rightfully have been registered about excessive time spent by patients in waiting to see us. Most of us know how this excessive waiting time can be reduced in our own offices, but too often we fail to take the steps to correct the problem. Remember, the situation is not going to get better without your attention. Our survey shows that patients are complaining twice as much about long waiting as about fees.

"There is no excuse for 'standing room only' in reception rooms. Even when emergencies arise, our assistants can explain graciously what has happened. Then perhaps new appointments can be made or patients can be asked to return in an hour or so. Another practice I personally deplore is that of allowing the preferred patient to come in the back door ahead of those persons waiting in the reception room. Patients are wise. They know what is going on and resent it. If you want to do something special for your friends, that is fine, but do not do it at the expense of the other patients in the waiting room. By reducing the amount of waiting time in the reception room, we will benefit too. There will be less patient criticism, and we will find them more composed and co-operative when we do get to see them."

Let us continue with Dr. Murray as he comments on the charge that doctors are not sufficiently frank with patients.

"Another complaint of our patients is the lack of frankness and honesty in explaining the diagnosis, the treatment or the surgery performed. The American people . . . [insist] on facing reality rather than running away from it. This desire has become a part of the make-up of most Americans. In everything in which we participate we insist on knowing the full story.

"So when a doctor tells a patient, 'Don't worry about a thing,' he is not fostering good doctor-patient relationships. Why should a patient accept such a vague statement? His health is his personal concern, and he should know if he has a disease or if he has not, if he needs an operation or if he does not. We need the patient's co-operation, assistance and agreement if we are going to help him. We cannot get this if we are constantly hedging and giving general, rather than specific, answers to his questions. Our diagnosis should be explained so that the patient has a clear concept of his illness, its nature, and its course. Absolute honesty and frankness in this matter will be appreciated by the patient.

"If an operation is necessary, some of the basic details should be given to the patient. Certainly, after the operation the doctor should explain carefully to the patient exactly what has been done and why. There are extreme cases, of course, when the full story cannot be told to the patient, but in these cases a relative or close friend of the patient should be informed. Thus, in almost all cases the patient has a right to know. He comes to us in the first place because he is concerned about his physical condition. He comes voluntarily, ready to pay for our services. He has the right to know what we have discovered about him, and whether it is good or bad news."

The criticisms which indict the doctor on economic grounds are discussed in the next section.

#### THE ALMIGHTY DOLLAR

Doctors interviewed in the A.M.A. survey correctly anticipated that the public would be critical of them for high fees. We find the following criticisms by non-medical interviewees:

1. Doctors charge too much.
2. Doctors have raised their fees too fast.
3. Doctors make too much money.
4. Doctors plan to get rich quick.

The solution to this problem is complicated by Dr. Murray's observation that "in making judgments people invariably employ themselves as a frame of reference and, as most people's occupations do not require long and



expensive training and as they are not as well rewarded financially, they naturally feel that doctors charge and make too much."

He makes the further statement that "the public has been taught that age and experience rather than training and ability are the cost determinants of service. Young doctors (lacking the age and the experience the public expects) are probably the group most frequently accused of get-rich-quick practices."

Organized medicine through its national and regional public relations program can help shift the unfavourable opinions of the economic side of medicine by a large segment of the public, but, as in all aspects of medical public relations, the biggest job can be performed in the doctor's office—at the point of contact. Rather than consume space here with a discussion of how the collision between the human side and the business side of medical practice may be softened, we would refer the reader to an earlier article in this column, "Doctors and Dollars".\*

A major criticism under this heading cannot be ignored. About one-third of the respondents accused doctors as a group of charging higher fees for services covered by medical care insurance. The disturbing factor is that 18% of the doctors surveyed agreed. Only the inveterate idealist would believe that such a practice can be eliminated completely. However, if the doctors believe in the principle of insuring against the cost of medical care and view such insurance as a bulwark against the incursion of government control, then each must make every effort to curb unwarranted abuse of medical care insurance plans and the policy holder. A determination not to charge the plan more than he would have charged the patient is the golden rule in third-party dealings.

IS THIS YOU, DOCTOR?

OR

IS YOUR HALO GETTING TIGHT?

(The following is an excerpt from a speech quoted in *Secretary's Letter*, published by the American Medical Association.)

"The ideal physician must, of course, be of fine and scholarly appearance, with great intellectual capacity, of faultless personal habits, and inspire the confidence of his patients and the respect of all others.

"He must be active in community affairs, taking his full part in Chamber of Commerce and service club functions, serve on and advise municipal and other governmental bodies as called upon, be active in local and state political affairs, be a good church worker and attend church frequently.

"He must be available on short notice for papers to local PTA and church groups, service and business girls' clubs, and all other groups and organizations

interested in obtaining reliable information on medical subjects. He must, of course, take an active part in the various youth programs of the community.

"He must work on and contribute liberally and cheerfully to fund raising campaigns for new hospitals, YM and YWCAs, old peoples' homes and nursing homes, give liberal support to the church and community chest, and help defray the deficit of the local ball club.

"He must be active in his local and state medical societies, attend meetings regularly, and accept officership and committee assignments eagerly and perform his duties quickly and with great tact and diplomacy.

"He must be faithful in attendance at hospital staff meetings, be ready to give carefully prepared scientific papers, serve on hospital committees cheerfully and efficiently, keep his hospital records complete in all details, and be prompt with carefully prepared lectures to the student nurses.

"He must be a good family man with a gracious and tactful wife who abhors mink coats and other vulgar extravagances, and must spend lots of time at home with his children.

"But above all this, he must never fail to give his patients the finest possible medical service, keeping abreast of medical progress by reading, attendance at medical meetings, and taking frequent post-graduate courses. He must be a tireless worker and improve his public relations by spending adequate time with his patients, answering urgent calls promptly, day or night, and by not keeping his patients waiting. This must all most certainly be done for what has been vaguely defined as a reasonable fee."

#### FOR YOUR PATIENTS

During mid-December the *Toronto Globe and Mail* published a series of 12 medical articles prepared at the request of the Canadian Medical Association. The following subjects were discussed in non-technical language: The Menopause; Food Poisoning; The Thyroid Gland; Plastic Surgery; Allergy; Hypertension; Poor Eyesight; Varicose Veins; Poor Hearing; Accidental Poisoning in Children; Heart Disease; Epilepsy.

Reprints of any or all of these articles are available from the Promotion Department, *Globe and Mail*, Toronto, Ontario.

The doctor may find that a supply of these reprints at hand will be of value in helping some patients understand their illnesses.

#### VOICE OF THE PUBLIC PRESS

*Labor for health plan*—Canadian labor groups are going all out this year to fight for a national health plan. This was pointed up by the Manitoba Federation of Labor meeting in Winnipeg last month. Greatest opposition to a health plan is coming from the insurance companies, "the real enemy of labor in labor's health program." (*Winnipeg Free Press*)

*Manitoba reluctant*—According to Robert Bend, Manitoba's Health Minister, his province finds some sections of the Federal government's hospital insurance proposals "unacceptable." Tuberculosis and mental illness should be a Federal responsibility. Responsibility for Indians under the national plan would be shifted from the Federal to the provincial government, the health minister added. Earlier reports indicate that Manitoba would prefer a scheme of catastrophe insurance rather than the more extensive plan proposed by Ottawa. (*Winnipeg Tribune*)

\*Canad. M. A. J., 73: 981, 1955.

*C. of C. reiterates stand*—The Canadian Chamber of Commerce, long the champion of free enterprise, sees the Federal government's proposed hospital insurance scheme as the first step toward a "state medicine."

"Any financial assistance provided by the federal government should be directed to areas in which the individual is generally unable to help himself, to the indigent, the aged, the chronically ill and to those who suffer catastrophic medical expenses," the Chamber believes. (*Winnipeg Tribune*)

*"Free" hospitalization?*—According to an official of the Department of National Health and Welfare, quoted in *The Ottawa Citizen*, the Federal government's national hospital insurance program "simply provides financial assistance to the provinces to enable them to carry out a scheme of free hospitalization for their populations." Paradoxically he pointed out the plan will cost close to \$1,000,000 per day.

## Men and Books

### SURGERY, SCIENCE AND HUMANITY\*

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THE PRACTICE of medicine or surgery today, as compared with practice as recently as 50 years ago, while identical in fundamental philosophy and obligation, has become complicated by many changes. These changes include specialization, great scientific advances, economic changes, organizational developments and some rather basic changes in other organized societies and governmental policies, to mention only a few. These new influences on the practice of medicine and surgery which have developed largely during the present century have made it even more necessary to take an occasional introspective glance for the purpose of self-evaluation if proper balance is to be maintained within our profession.

Characteristically, we are always looking forward, but past experience is perhaps our most valuable teacher. Therefore, it might be worth while to look backward for a moment, as among our predecessors were many men of sterling qualities and abilities to whom we are tremendously indebted. At the turn of the century the doctor necessarily relied heavily on information gained through his five senses. They were an invaluable source of supply and one which today may suffer somewhat from atrophy

of disuse because of competition from batteries of laboratory tests and other diagnostic procedures. With the relatively meagre developments of biochemistry and physiology of 50 years ago as compared with those of today, the doctor naturally thought more of his patient and less of his patient's constituent parts. He thought of the patient as a person—of his worries, his comfort, his personal problems and his responsibilities. The patient did not represent primarily a disease entity but an individual who was ill and needed help. This help was offered happily and willingly, day or night, and with the humility of Ambroise Paré as expressed in the words: "I dressed the wound: God healed him." The doctor's thoughts were directed primarily towards service and care of patients, not primarily towards financial gain, personal security or fewer night calls. The doctor of those days had no need for protective insurance, as seldom if ever would one think of suing a loyal friend, diligent worker and justifiably respected member of the community. Although his income in dollars may have been small, his returns in devotion and loyalty were large.

Committees on public relations were unknown and unneeded. Then, as today, each doctor was more significantly and effectively engaged in public relations work for the profession as a whole than any committee or other agency. He did a good though largely unconscious job in this regard. Although we may be conscious of these relations today, I am not sure that we always handle them well. With kindness, genuine concern for the patient's welfare, a feeling of responsibility for each individual patient and his family and evident friendly interest at all times, the doctor of yesterday generated a reciprocal feeling of affection and confidence on the part of his patients and the public at large. This was one of the profession's greatest assets. I wonder whether we can say the same today.

I know that you have all read at one time or another the book, *A Doctor of the Old School*, written some years ago by a minister of Liverpool under the name of Ian McLaren. I trust that you enjoy as much as I do rereading some of the passages of this small volume. If so, you will recall some of the following:

"It was impossible for a doctor to earn even a modest competence from a people of such scandalous health . . . His house . . . little more than a cottage . . . stood on the roadside among the pines towards the head of our Glen . . . where the snow drifts were twelve feet deep in winter and the only way of passage at times was the channel of the river . . . He did his best for the need of every man, woman and child in this wild, straggling district, year in, year out, in the snow and in the heat, in the dark and in the light without rest and without holiday for forty years.

"One horse could not do the work of this man, but we liked best to see him on his old white mare, who died the week after her master, and the passing of the two did our hearts good. It was not that he rode beautifully, for he broke every canon of art, flying with his arms, stooping till he seemed to be speaking into Jess's ears, and rising in the saddle beyond all necessity. But he could ride faster, stay longer in the saddle and had a firmer grip with his knees than anyone I ever met, and it was all for mercy's sake.

\*W. Fulton Gillespie Memorial Lecture at the joint meeting of the Faculty of Medicine of the University of Alberta and the sectional meeting of the American College of Surgeons, Edmonton, Alta., April 23, 1956.

†Section of Surgery, Mayo Clinic, and Mayo Foundation. The Mayo Foundation, Rochester, Minnesota, is a part of the Graduate School of the University of Minnesota.



"Before and behind his saddle were strapped the instruments and medicine the doctor might want, for he never knew what was before him. There were no specialists . . . so this man had to do everything as best he could and as quickly. He was chest doctor and doctor for every other organ as well; he was accoucheur and surgeon; he was oculist and aurist; he was dentist and chloroformist, besides being chemist and druggist."

I have been unable to learn who first mentioned the essential attributes of a good surgeon, namely the head, the heart and the hand, but these attributes are as essential today as when they were first mentioned. How do we stand today in regard to them?

There can be little doubt that the phenomenal scientific and technical advances that have been made in medicine and surgery since the turn of the century offer far greater opportunity for prevention and effective treatment of serious disease than was ever available before. Howard A. Rusk said last year that "two thousand years ago the average length of life was 25 years; at the turn of the century it was 49; recently compiled statistics of the National Office of Vital Statistics show the average length of life in the United States has now increased to 68." Actually, I believe that more recent figures show it to be even higher, but I am certain that with this audience I need not dwell on the numerous and far-reaching developments in medicine and surgery and their social as well as their economic significance. Obviously, we as members of the medical profession are equipped to do a better job than ever before.

This fact in itself brings certain problems. It is conceded that the doctor of today must constantly and eternally continue his education so that his patients may have the benefit of all the rapidly developing advances both technical and scientific. E. R. Samuel, who last year was elected by the American Medical Association as "General Practitioner of the Year," expressed the idea in this way:

"I sometimes think that a young doctor starting out is like a new grocery store. There are a lot of fancy goods on the shelves. But they start to go and have to be replaced. The merchandise on the doctor's shelves is new knowledge."

If this meant only reading medical literature and attending medical meetings it would perhaps not be too difficult. But there is more involved. As stated recently by Frank C. Mann:

"If the medical practitioner is to give his patient the benefit of the advances in his profession and at the same time protect the patient from unwarranted experimentation, he must be able to judge between the true and the false in the mass of reports of new discoveries that reach his desk in his journals and are presented at the meetings of his professional societies. A period of time in a research laboratory affords the young physician the best training for correct evaluation."

Speaking of medical and surgical literature, K. B. Castleton, in an editorial that as yet is unpublished, emphasizes a matter of growing importance. He states:

"It is not an uncommon experience for a general surgeon in private practice to read or to hear a favorable report by a surgeon of national repute regarding a new surgical procedure or technic, to try out this procedure only to learn that the late results are not as favorable as the immediate results would indicate and on investigation to discover that the procedure has already been discarded by the original author without any retraction of his earlier favorable comments on the subject . . . The undesirable aspects of this situation are multiple in that there is at times too great haste on the part of some in reporting new developments and procedures whose values have not been established and secondly a reluctance to report unfavorable results and thereby reverse a previously stated opinion."

If the surgeon who first reported the procedure would be in as great a hurry to report his poor results as he was in presenting his initial report, much of this difficulty would be avoided. Preliminary reports should be accepted for what they are and should not incite all who hear them to abandon well-established surgical practices for something of unproved value. Likewise, care should be exercised by those who are in a position of professional prominence not to discuss and advocate the developmental and perhaps theoretical procedures on which they are working in a manner that gives them the stamp of their own authoritarian approval for widespread clinical use. The shoe fits both the foot of the professor and the foot of the individual surgeon.

The value and importance of research are obvious to all. Research in medicine is a continuing search to discover nature's previously unrevealed secrets so that care of the sick may be improved. Research may be basic or applied, and both are essential. The fruits of these efforts constitute the improved treatments of tomorrow. Winston Churchill is quoted as saying that "science is no more than organized curiosity". True, we are likely to think of research as requiring extensive facilities, expensive equipment, an intellectual environment and plenty of time. No doubt this is true for what might be termed "big-scale" research. On the other hand, an inquisitive mind, interest and commonly possessed basic knowledge of pathological physiology provide any of us with the essentials for making a significant observation or developing a train of thought that might form one part of an important discovery. Obviously we all encounter a sufficient number of unsolved problems each day of our lives to serve as a stimulus in the quest of new knowledge and to pose an unanswered question for the researcher in applied sciences.

One entry should be made on the other side of the ledger, however. With the multitude of research programs being conducted in medicine

and surgery during recent years and the enthusiasm which they generate, perhaps a few of us are too prone to carry the spirit of research to the bedside or the surgical amphitheatre. True, surgical progress must be made at some time by initial efforts in the operating room, but these efforts should not be made lightly or until the justification and advisability of a given surgical innovation have been determined on the basis of careful humanitarian thought, logical reasoning and controlled observations in the laboratory. No human being is an experimental animal, and let us not confuse the operating room in the hospital with that of the experimental laboratory. The radical and extensive surgical procedures that are recommended today by some surgeons may have occasional indications in the hands of the experienced, but this does not mean that they should be employed universally. There is, of course, no substitute for skill and surgical judgment, the acquisition of which requires strict discipline, adequate training, a certain amount of mental competence and prolonged effort.

Turning now from the head and the hand to the heart, one might ask: Have we, with all these scientific and technical developments of the past half a century, lost anything of value? Have the remarkable advances in medicine and surgery resulted in direction of thought and action so that we are too inclined to look upon our patients only as so many milliequivalents of potassium, so much extracellular fluid, a problem in nitrogen balance, a diagnostic puzzle or a surgical challenge? Such considerations are essential in the present-day care of patients, but do we at times forget that "the patient, not the disease is the entity"? With the expanding sum-total of medical knowledge, an increasing degree of specialization has become necessary, particularly in large cities and medical centres. Has this development resulted sometimes in a number of doctors being interested in small parts of the patient but no one really considering the patient as a whole—as a person who is sick and perhaps needs help in ways other than just medical diagnosis and treatment? It might be asked also whether economic considerations, personal interests and the rush of busy schedules have made us less mindful than our predecessors of the human side of our obligations. Undoubtedly many of the changes in the practice of medicine and surgery that have occurred in recent years have been the result of changing economic, social and governmental influences in our own and other countries. These factors, even though beyond our control, need not change our basic ideals as doctors or alter the significance of the Hippocratic oath. If we are constantly guided solely by what is in the best interest of the patient we will commit no blunder or errors that our abilities permit us to avoid.

As usual in any consideration of the practice of medicine and surgery, heavy responsibilities are assigned to the leaders, the teachers and the professors who enjoy the privileges but also the duties and obligations of teaching students, interns and residents as well as younger associates. If we are not careful, years of institutional training may lead the young surgeon to consider that he is treating diseases rather than patients. Unless some thought is given to the matter, he may grow to consider a patient as "the common-duct obstruction in bed 6" rather than Mrs. Thomas, the mother of four children who appears to have biliary obstruction.

Let us not forget that the junior man absorbs from his senior not only his scientific approach, surgical judgment and details of technique; the junior absorbs also something of his chief's character, his inquisitive mind, his possession of or deficiency in fundamental honesty, his kindness or lack of it, his attitude towards patients, rich and poor, his appreciation of obligations to patients, colleagues and society, his moral courage and the many other attributes that characterize the individual surgeon. There is no doubt that responsibilities to our juniors are great and of this we should always be mindful. Speaking of the rich and poor, it is well to remember that although there may be some distinctions between the ward patient and the private patient, our fundamental duties and responsibilities are identical with respect to both. Actually, of course, the ward patient is frequently more in need of personal consideration than the possessor of a well-filled pocket-book who occupies a large private room. As Julian Johnson recently stated:

"My surgical residents have repeatedly been told that there is only one inflexible rule on my service, namely, that every patient either ward or private, regardless of race, color or creed, be treated as if he were a member of his family or indeed as he himself would want to be treated under such circumstances . . . I believe that a chief should never leave a resident with an operation until he feels that resident can do the operation as well as he can . . . Unless the resident has seen the procedure often enough and has been 'nursed through' it often enough to feel at home with it, he should not be left alone. The primary objective of any teaching hospital is to give its patients the very best care, regardless of their economic status. Only by so doing can we give our young surgeons the desire to do likewise."

Perhaps group discussions and seminars on some of the broader, non-technical aspects of medical practice have not received sufficient attention in our medical schools and residency training programs. Subjects for such discussions might include: medical ethics, the doctor's role in his community, industrial surgery, surgery in a large city, general practice, surgery in county areas, academic careers, research careers, group practice, government medicine, economic aspects of medical care, partnership in medical



practice and many other subjects. A curriculum filled only with scientific teaching and training just partially equips the young graduate for his future career.

One word about the financial aspects of medical practice today. Comments are made frequently about the high cost of medical and surgical care, a good share of which actually is the cost of hospitalization. Much but not all of this is beyond our control, but it seems only reasonable that we should be sincerely interested in this problem and do what we can to reduce excessive expense. I refer to our own daily practice. After all, everything that we use in the care of patients—laboratory tests, x-ray examinations, dressings, sutures, blood for transfusion, instruments, solutions for intravenous administration, drugs, antibiotics, periods of hospitalization and all—costs money that someone must provide. This someone is either the patient or the taxpayer, as a rule. We do not pay for these things directly ourselves but it might be well if we used them as though we did. On the other hand, thoughts of personal gain should not cause us to change the art of medicine into the business of medicine. In the words of Sir Thomas Browne, "No one should approach the temple of science with the soul of a money changer."

I fear that after these somewhat varied remarks I may have placed myself in the category of the politician who for a considerable period had been addressing a large crowd at a political gathering in the state of North Carolina. A newcomer to the scene turned to a local farmer on the fringe of the crowd and asked:

"Is he making a good speech?"

"He's making a fine-sounding speech," the farmer replied.

"What's he talking about?" asked the newcomer.

"He ain't said yet," replied the farmer.

Perhaps I might not do better in concluding these remarks, which perhaps would have been more fitting in the United States than in Canada, than to suggest that we all diligently endeavour to exemplify the physician described in the often repeated quotation from Stevenson:

"There are men and classes of men that stand above the common herd: the soldier, the sailor, and the shepherd not infrequently; . . . the physician almost as a rule. He is the flower (such as it is) of our civilization; and when that stage of man is done with and only to be marveled at in history, he will be thought to have shared as little as any in the defects of the period and most notably exhibited the virtues of the race."

In a word, I am suggesting that we lead our lives and practise our profession in a manner which I am sure would merit the approval of Dr. W. Fulton Gillespie.

## GENERAL PRACTICE

### SOME PROBLEMS IN PÆDIATRIC GYNÆCOLOGY\*

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PÆDIATRIC GYNÆCOLOGY has long been a neglected aspect of the practice of both pædiatrics and gynæcology. Contrary to the generally held impression, symptoms relative to the genital tract are not uncommon in girls within the pædiatric age group. The complaints are often mild, and findings frequently merely represent variations in the pattern of normal development. Organic lesions, both congenital and acquired, however, do occur and must be recognized, as they deserve consideration in a variety of clinical situations.

In comparison with other body systems, growth and development of the female genital tract are relatively late. Function of the reproductive tract is usually associated with the years which follow rather than those which precede puberty. Because of these factors, there has been a tendency on the part of both parent and doctor to exclude this important system from consideration and examination.

#### HISTORY TAKING AND PHYSICAL EXAMINATION

The management of a gynæcological complaint in a prepubertal girl demands more than the usual amount of tact and understanding on the part of the physician. Anxiety in the mother is often unnecessarily exaggerated because of the fear of an unwholesome origin of the disorder or fear of its possible implications regarding the reproductive future of the child. Unfortunately, emotional reactions of the parents are readily transferred to the child. At the outset, the child is frequently less disturbed by the complaint than is the mother but, later, sensing the reaction of her parent, she may have a similar emotional response. Frequently it is better, having received the parent's version of the history, to conduct the remainder of the examination apart from the mother with the child in the care of a sympathetic nurse. The value of the child herself as a source of details of history should not be underestimated.

In the past much has been said about the physical and psychological trauma that may follow examination of the genital tract of the immature girl. The justification of these claims has never been established; in fact, it has been abundantly shown that no undesirable sequelæ

\*Read at the Annual Meeting of the Canadian Medical Association, Quebec, June 1956.  
This is a condensation of the chapter on Pædiatric Gynæcology from *Pediatrics*, ed. Paterson and McCreary, Lippincott, Philadelphia, 1956.

occur. The presence of an intact hymen should not prevent the careful examination of the upper vagina when the indications for such an examination are present. With patience and gentleness the upper vagina can be explored digitally or with a culture swab without physical injury or serious discomfort. The immediate and delayed reaction of the child is frequently no more than that which accompanies examination of the ears or throat. Much greater harm, both physical and psychological, is likely when a necessary examination or treatment is withheld because of ill-founded superstition. Only when unhealthy attitudes and false ideas are allowed to persist in the mind of the parent are unfortunate psychic consequences to be expected.

The placing of the child for examination can be in one of three postures: the dorsal, the side, or the knee-chest position. The dorsal, or lithotomy, position is preferred by most doctors because they are most familiar with anatomical relationships in this approach. Many, however, feel that less disturbance is caused to the patient when she is lying on her side or is in the knee-chest position. With practice, success can be achieved by any of the three methods and the choice is largely one of personal preference.

Certain anatomical differences in the genital tract exist between the adolescent and mature female. The genitals of the immature individual are more prominent because of the absence of a fat pad within the labia majora. The introitus is more anteriorly located than in the mature woman. The visible mucosa is often red in colour due to the thinness of the surface epithelium, and this does not necessarily indicate an inflammatory reaction. The labia minora are usually prominent. Extreme gentleness is essential as even light touch produces an exaggerated response in the highly sensitive area about the hymen. Firm lateral pressure applied to the outer aspects of the labia majora on either side will expose the hymen area without discomfort.

In very young children, vaginal examination is not possible without anaesthesia. However, with gentleness and the use of the smaller fifth finger instead of the index finger, it is possible in the older preadolescent to perform a satisfactory digital vaginal examination. One may be impressed with the apparently exaggerated length of the vagina. This is partly due to the fact that the pelvic viscera are higher within the pelvis than after puberty. The anterior and posterior fornices are not well developed, making it impossible to pass the examining finger high enough vaginally to outline the other pelvic structures.

Rectal examination provides very useful information in children of all ages and in younger children it must frequently suffice. Here again it may be necessary to use the fifth finger although the index finger generally provides more

useful information. It is usually possible to outline the uterus as a small, mobile mass. Only rarely are tubes and ovaries palpated. The uterus lies in a position in line with the axis of the vagina rather than in the anteflexed position common in the adult. Prior to puberty the cervix exceeds in length the body of the uterus. In the mature woman this situation is reversed. Only very rarely should the diagnosis of infantile uterus be made even in a girl at puberty. Delayed growth of the uterus is common and requires no specific therapy if other evidences of maturity have progressed as expected. The premature administration of hormones and the expression of potential difficulties with fertility or childbearing are to be avoided.

Frequently a combined rectovaginal examination will be effective and less disturbing to the patient than a vaginal examination alone. With one finger inserted into the rectum, a small metal instrument or catheter can be passed into the vagina with a minimum of further discomfort. This technique is very useful in exploring the vaginal tract for foreign bodies and in the taking of cultures. The rectal finger distracts the child so that she is less sensitive to the insertion of an instrument into the vagina.

Visualization of the upper vagina and the vault can be accomplished by passing a Kelly air cystoscope, an infant laryngoscope or a small Sims speculum. An elongated nasal speculum is useful in the very young. Instruments should be warm and kept out of sight until used. The knee-chest position is considered best for visualization because of the "ballooning out" effect of the vagina which occurs with this posture.

It should be noted that most gynaecological problems can be met by standard forms of physical examination and the employment of a minimum amount of specialized equipment. In some patients within this age group, it is impossible to perform a satisfactory examination without the relaxation afforded by anaesthesia. When necessary to provide essential information, such a procedure is justified.

#### EMBRYOLOGY OF THE FEMALE GENITAL TRACT

During the second month of gestation, four parallel, bilaterally symmetrical tubes grow caudally in the subperitoneal tissue of the posterior abdominal wall. The lateral pair are the Wolffian or mesonephric ducts and the medial two are the Müllerian ducts. In the female the mesonephric ducts almost completely disappear, persisting only as rudimentary vestiges without function. From the Müllerian ducts develop the Fallopian tubes, the uterus, and most of the vagina. The cephalic portions of the Müllerian ducts remain unjoined, forming the Fallopian tubes. The intermediate and caudal portions converge and later fuse in the



midline forming, the body of the uterus, the cervix, and the upper four-fifths of the vagina. The lowest part of the vagina and the external genitalia are derived from the urogenital sinus. Initially a solid plate of cells, the vaginal plate, separates the upper and lower vaginal components. Later this plate, too, becomes canalized, rendering patent the entire vagina.

The ovary develops from the genital ridge on the ventral surface of the mesonephron.

#### CONGENITAL ANOMALIES

Congenital anomalies of the female reproductive tract are not infrequent. These abnormalities may present as an obvious deformity at birth or their recognition may be delayed until full maturity. A number of different abnormalities of fusion of the two Müllerian ducts have been described leading to structural variations of the uterus, cervix, and vagina. These are usually detected only when they produce disturbances of childbearing function and rarely present problems within the paediatric age group.

It will be noted how closely the genital tract is allied in its origin and development to that of the urinary tract. Frequently congenital abnormalities of one system occur simultaneously with defects in the other. A full urinary tract examination, including pyelography, is indicated in the investigation of any major abnormality of the female reproductive system.

*Imperforate hymen* is one of the more common congenital anomalies encountered. It is due to a failure of communication between the canalized caudal portion of the Müllerian ducts and the invaginating portion of the urogenital sinus which forms the inferior end of the vagina. The hymen, a cuff-like circular fold of skin at the lower end of the vagina, normally has one or more openings which allow the free drainage of secretions. An imperforate hymen usually is recognized only when there is retention of such secretions within the vagina. Rarely this obstruction of the genital canal leads to a *hydrocolpos* or *hydrometra* in infancy, where retained watery or mucoid secretions distend the vagina and uterus. Much more commonly, recognition occurs shortly after puberty when retained menstrual blood produces a *hæmatocolpos* or *hæmatometra*. This complication is suggested by the delayed onset of menses in an adolescent girl and crampy lower abdominal pain that may be recurrent at approximately monthly intervals. Disturbances of micturition are sometimes described. On examination the diagnosis is usually apparent. A bulging hymen is seen which, if thin, will appear blue. When the vagina or uterus is markedly distended, a suprapubic mass can be outlined. Rectal examination reveals a tense, fluctuant swelling filling the pelvis. Treatment consists of wide incision

of the hymen to allow free draining of the retained vaginal contents. As infection is always a danger, vaginal examination at time of drainage is contraindicated.

#### PHYSIOLOGICAL DEVELOPMENT OF THE GENITAL TRACT AND SOME COMMON ABNORMALITIES

Development of the reproductive tract is not a steady process dating from birth and progressing evenly towards puberty. Following a long period of initial quiescence, gradual growth begins at approximately the age of nine. The rate of development occurs at an accelerated pace in the year or two preceding puberty. The term "puberty" is used to denote the interval of time during which secondary sexual characteristics make their appearance. "Menarche" refers to the time of onset of the first menstrual period.

The endometrium of the uterus is under the influence of the oestrogenic stimulus. Preceding puberty there is a fluctuation in the oestrogen level which is secondary to a more or less cyclical fluctuation in the output of pituitary gonadotrophins. Gradually the levels of circulating oestrogen become sufficiently great so that at the time of a regular decline in the oestrogen level, a vascular crisis appears and menstrual bleeding occurs. Initially bleeding appears without ovulation having taken place. Gradually, however, with increasing maturity of the endocrine control, oestrogen production reaches a level adequate to stimulate the release of luteinizing hormone from the pituitary, leading to ovulation and secretory change in the endometrium prior to breakdown.

The time of onset of bleeding, known as the menarche, is very variable and frequently is more closely related to the stage of physical development than to chronological age. Short, stocky girls tend to menstruate earlier than tall, slender girls. The menarcheal ages of mothers and daughters have been shown to be directly related, and the difference between the ages of the menarche in sisters is less than in unrelated groups. During the early months of menstrual function, it is noted that seasonal influences may play a part. It is not uncommon for periods to be missed during the summer months, and during this season fewer girls than would be expected have their first episode of bleeding. In North America the average age of the menarche is 13½. An onset any time between 10 and 17 years is commonly noted and is regarded as being within normal limits.

*Precocious puberty*, or the appearance of secondary sexual characteristics before an arbitrarily selected age of nine years, occurs rarely. Most cases are due to a constitutional premature maturation of the endocrine control of the genital tissues. The changes represent perfectly

normal pubertal development which occurs at an abnormally early age. Less commonly, precocious development may be associated with a central nervous system lesion which characteristically involves the hypothalamus or the floor of the third ventricle. Menstruation in these two types is associated with ovulation. The third and least common cause for precocious secondary sexual development is a feminizing tumour of the ovary or adrenal cortex. The significant difference between this group and those previously described is that here the changes are entirely due to primary oestrogen production and are not secondary to early activation of other endocrine glands.

Young children showing these early changes warrant examination to exclude neoplasm or central nervous system damage. If no definite pathology is found, they can be considered as belonging to the constitutional or idiopathic group. For these cases, treatment is unnecessary. The nature of the disturbance should be explained to the parents and eventually to the girl so that the latter may grow up normally, free from possible psychological stigmata that may accompany a misunderstood physical aberration.

Intervals of *secondary amenorrhœa*, or missed periods occurring after the menarche, are not uncommon. Constitutional causes such as anaemia or undernutrition may be responsible and should be corrected. Frequently, psychic factors, associated with increased tension or new responsibility, bring about a temporary disturbance of the pituitary-ovarian axis that is manifest by amenorrhœa. Changes in climate or environment may produce a similar effect. These disturbances are generally self-limited and treatment is unnecessary. When a psychic factor can be recognized, explanation and reassurance are of value.

The *delayed onset of the menarche*, or *primary amenorrhœa*, is common and should not be a cause for anxiety before the age of approximately 17. Prior to this age, a complete assessment of the general physical and nutritional status of the girl, with particular attention to developmental abnormalities of the reproductive tract, is indicated. However, if these investigations fail to reveal causative lesions, an optimistic expectant attitude should be maintained. A logical plan of investigation which attempts to localize the defect in the endocrine chain is justifiable, but undue stress on the abnormality, and the submission of the patient to elaborate laboratory investigations and expensive treatment, are indicated only in the exceptional case.

Variations in the menstrual pattern, which may take the form of profuse, prolonged, or irregular periods, are common in the early stages of menstrual function. These disorders are rarely serious and represent merely a

transient phase in the gradual development of a mature endocrine balance. Regular cycles may not occur for 18 months or longer after the menarche. Chief stress in management is placed upon systemic factors including improved habits of rest, diet and exercise, and the correction of anaemia. Occasionally, when blood loss is profuse and does not respond to the measures outlined, a plan of cyclical endocrine therapy, employing oestrogens (oestrone sulphate or stilboestrol) and progesterone, will prevent prolonged periods of unopposed low-level oestrogen stimulation which result in endometrial hyperplasia and irregular bleeding. Dilatation and curettage is reserved for those rare cases where blood loss continues despite all medical measures.

*Dysmenorrhœa*, although a common complaint in the late teens and 20's, is not a major problem of girls in the adolescent years. When it occurs, it is commonly of the primary or idiopathic type. Organic lesions, such as cervical stenosis, vaginal atresia, and imperforate hymen, which obstruct drainage of the menstrual blood, account for only a small percentage of cases. One of the reasons why painful periods are infrequent in the months that follow the menarche is that at this time ovulation frequently does not occur. Although the explanation is not clear, it is well recognized that primary dysmenorrhœa occurs only in the presence of ovulation and a secretory endometrium. Psychic factors, often unwittingly implanted in the mind of the child by the mother, are frequently involved with painful menses in this age group. Explanation of the purpose and physiology of menstruation will serve to allay anxieties and dispel misconceptions in the mind of both the patient and her mother. The girl should be encouraged to continue her regular activities during the menstrual flow. Moderate forms of physical exercise are permitted. Mild sedation without narcotics can be used in more resistant cases.

*Pregnancy* is not rare in girls in their early teens. This is in spite of reduced fertility at this age because of the occurrence of anovulatory periods. In general, adolescent girls tolerate pregnancy and labour well.

#### SOME COMMON GYNÆCOLOGICAL COMPLAINTS

*Vaginal discharge* accounts for a high proportion of the children brought to a doctor for gynecological examination. A careful history must be taken regarding recent infectious disease in the home, habits of cleanliness, and a detailed description of the discharge. With vaginal discharge, perhaps more than with any other gynecological complaint, the mother's history is likely to be distorted or exaggerated. The doctor must satisfy himself on the evidence available by examination rather than accepting



the history without reservation. Underclothing often provides the best evidence as to colour, consistency, and odour of the discharge. On examination of the patient, the external genitalia are inspected for concretions, discharge, and evidence of inflammation. The hymenal area is exposed by firm lateral pressure on the posterior portion of the labia majora, using the index and middle fingers of the left hand. Cultures should be taken routinely, employing a tightly wrapped cotton applicator or glass catheter. One finger in the rectum helps to control and guide the direction and depth of insertion into the vagina. In the younger child, discharge can sometimes be "milked out" of the upper vagina by a rectal finger.

Not all vaginal discharges are secondary to infection. A thin, white, odourless discharge may be seen in the adolescent girl which is unaccompanied by itching or evidence of irritation. This non-infective secretion is believed to represent an exaggerated response of vaginal and cervical epithelial cells to the oestrogen stimulation which precedes the menarche. The diagnosis is made after careful examination and cultures have excluded infection. Smears show well-cornified epithelial cells with relatively few leukocytes. Explanation and reassurance as to the benign and transient nature of the complaint should be given. Local cleanliness is all that is usually required in therapy.

Apart from the exception already described, vaginal discharge is most commonly associated with a vaginal infection which may have a specific or non-specific origin.

Specific types of vaginal infection:

(a) Gonorrhoeal vaginitis was one of the commonest causes of discharge in children prior to the era of sulphonamides and antibiotics. Epidemics were seen in schools and institutions. Now only rarely is the classical picture of a vulvovaginitis, proctitis, and profuse purulent vaginal discharge found. Parenteral penicillin promptly clears most cases. In resistant infections oestrogens given orally lead to cornification of the vaginal epithelium and increased local tissue resistance. Stilboestrol 0.1 mg. per day for ten days is recommended.

(b) Streptococcal vaginitis may be seen in children who have had systemic streptococcal infections such as scarlet fever. A thin, watery discharge that may be blood-tinged is characteristic. Penicillin is very effective in therapy.

(c) Monilial vaginitis usually is seen in children who are diabetics. There is a white, cheesy discharge associated with a marked vulvovaginitis. Treatment is facilitated by improved control of the diabetic state. Gentian violet, in 1% solution or in jelly form, is an effective local remedy.

(d) Trichomonas infection is rare but may be found in older children. A frothy green discharge with a pungent odour should suggest this

possibility. Microscopic visualization of the motile pear-shaped protozoal organism in a fresh saline suspension confirms the diagnosis. Treatment with an anti-protozoal agent such as Devegan vaginal suppositories should be given. The tablets may be broken in half before use. They are more easily inserted after moistening with water.

Non-specific vaginal infections, most of which are secondary to some irritating factor such as a foreign body within the vagina or a pinworm infestation, account for a large group of cases showing vaginal discharge. A discharge that is associated with intermittent bleeding or pain is highly suggestive of the presence of a foreign body. A wide variety of objects such as safety pins, stones, and pieces of wood may be introduced by the preadolescent child into her vagina. Diagnosis is best made by direct visualization using an instrument such as has been described. An x-ray of the lower abdomen will reveal a radiopaque object but may fail to show one that is of low density. Rectal examination is very helpful as the foreign body may be palpated through the rectal wall. In the removal of such objects, an essential part of the treatment of the infection, the rectal finger is helpful as a guide to the exploring vaginal instrument. Vaginitis may also result from the irritation of tight or unclean underclothing and from poor personal hygiene. Children should be taught to bathe adequately and following defaecation to wipe themselves from the front backwards.

Non-specific vaginitis should be treated with regard to the organisms grown on culture. As a rule a mixed group of bacteria, usually containing *E. coli*, is found. A wide-spectrum antibiotic given orally is preferred. With resistant infections, oestrogens as described under gonorrhoeal vaginitis should also be employed. Sitz baths are an effective and soothing form of local therapy. Potassium permanganate solution baths, two grains to one quart of water, are recommended.

*Fusion of the labia minora* (labial synechia) is an uncommon but dramatic condition that simulates a serious developmental anomaly. It is characterized by a midline adherence of the two labia minora to form an intact surface that occludes the lower end of the vagina distal to the hymen. A small opening is usually present anteriorly which permits the escape of urine. Careful inspection of the genitalia will reveal a white or bluish line extending backwards in the midline from the anterior opening. The condition may be congenital but more commonly results from postnatal irritation or infection. The diagnosis is usually made in infancy but recognition may be delayed for several years. Frequently the abnormality is discovered when a urinary tract infection develops as a result of obstruction of urine flow or because a small amount

of urine is held behind the membrane leading to infection and local reaction. It is important to recognize the condition and to distinguish it from congenital absence of the vagina. Once the diagnosis is made, the correction is simple and often can be carried out in the office without anaesthesia. Treatment consists of separating the fused labia along their line of midline cleavage. A lubricated probe or haemostat is inserted into the opening at the anterior limit of the adherent labia. A quick backward pressure results in the separation of the two fused surfaces, which then appear as reddened denuded areas but show minimal bleeding. The labia should be covered with a bland ointment and kept apart with a small amount of cotton for approximately two weeks to prevent refusion.

#### SUMMARY

In the practice of paediatric gynaecology, explanation and reassurance are the most frequently employed forms of treatment. Most minor aberrations of structure and function can be observed during this age group without resort to interference by surgery or endocrine therapy. In order to safely employ this conservative approach, the physician must be confident in his understanding of the anatomy and physiology of the reproductive tract during the developing years. Examination of the genitals should be made a regular part of a complete physical examination. Only by this means will the physician acquire the facility of technique and the familiarity with normal and abnormal findings that will enable him properly to diagnose and treat pathology when it presents.

#### RESIDENCY TRAINING IN GENERAL PRACTICE

N. N. LEVINNE, M.D., *Toronto*



THE COLLEGE of General Practice of Canada is an organization whose principal aim and purpose is medical education and—at the moment—on a postgraduate level. We are striving to produce, in Canada, a high level of

medical service, rendered by the family physician. We are trying to establish the family physician in his proper role, not only in relationship to his colleagues in the various specialties, but also in relationship to the family unit.

To properly act in the capacity of a family physician, a practitioner must be more than a good diagnostician and an adequate therapist. He must be able to serve efficiently as an adviser to a family unit, and as a manager of the team of patient, specialist and general practitioner, when this occasion arises.

This is an onerous task which befalls the family physician, not just on occasions, but almost daily, in the practice of his profession. The College takes great cognizance of the fact that the family physician has these three roles to serve, and is striving to establish in Canada, practitioners who will be able to meet these requirements. We want practitioners who will be able to justify the confidence the patient must have in his doctor; practitioners who will be rightfully accepted by their specialist colleagues in the performance of their services; and practitioners who will have the necessary pride in their own calling to adequately protect the health of the family unit for whom they are responsible.

To this end, the College of General Practice has established a Residency Training Program. At the moment there are about 22 hospitals from coast to coast in Canada which are making available the facilities required to carry out our program. Daily we are receiving requests from more and more hospitals to participate in this project. It is apparent that the profession is evaluating the importance of residency training in general practice, and is taking an active interest in its growth.

Residency training is geared to provide the fundamentals of a good family physician. Through the added year of hospital residency, greater skill will be acquired in diagnostic and therapeutic techniques. Through the added year of association with family physicians, and the preceptorship program, an introduction will be made to the role of medical adviser and team manager, which the young physician will be called upon to play.

It is the considered opinion of the College of General Practice that this will be more than a worthwhile experience for every young man who plans to enter general practice. The College encourages young men to seriously consider the advisability of a Residency Training in General Practice, so that they not only will elevate the standard of medicine in Canada, but also that they may enter this field adequately prepared and properly oriented.

The following hospitals are co-operating with the College by each establishing one or more Residencies in General Practice as of July 1, 1957:

#### ALBERTA

Misericordia Hospital, 9830 - 111th Street, Edmonton.  
Dr. A. J. Brunet, Medical Director.  
St. Michael's General Hospital, 13th St. and 9th Ave.  
S., Lethbridge. Sister M. Consolata, Administrator.



**BRITISH COLUMBIA**

Royal Jubilee Hospital, Victoria, B.C. Dr. J. L. Murray Anderson, Medical Administrator.  
St. Joseph's Hospital, Victoria, B.C. Medical Superintendent.

**MANITOBA**

St. Boniface Hospital, St. Boniface. Dr. Paul L'Heureux, Medical Director.  
Victoria Hospital, Winnipeg. Mrs. V. West, Superintendent.

**NEW BRUNSWICK**

Saint John General Hospital, Saint John, N.B. Dr. Carl R. Trask, Director.

**NOVA SCOTIA**

Aberdeen Hospital Commission, New Glasgow, N.S. Dr. H. C. McKay, Medical Superintendent.

**ONTARIO**

Belleville General Hospital, Belleville. Kenneth E. Box, Administrator.  
Hotel Dieu Hospital, Cornwall. Sister St. M. Magdalen, Administrator.  
Ottawa General Hospital, Bruyere Street, Ottawa. Dr. J. Paul Laplante, Medical Director.  
The General Hospital of Port Arthur, Port Arthur. J. A. McNab, Administrator.  
St. Thomas-Elgin General Hospital, St. Thomas. Bertram G. Thacker, Administrator.  
St. Joseph's Hospital, Sarnia. Sister M. St. Paul, Superintendent.  
New Mount Sinai Hospital, 550 University Avenue, Toronto. Sydney Liswood, Administrator.  
St. Joseph's Hospital, Toronto. Sister M. Estelle, Superintendent.

**QUEBEC**

Montreal General Hospital, Montreal. Dr. William Storrar, Medical Director.  
Notre-Dame Hospital, Montreal 24. Dr. J. R. Boutin, Medical Director.  
Royal Victoria Hospital, Montreal 2. Dr. R. V. Christie, Physician-in-Chief.  
L'Hôtel-Dieu de Québec, Québec City. Dr. J.-B. Jobin, Medical Director.  
Hôpital St-Joseph, 779 Ste-Julie, Trois-Rivières. Dr. J. J. Laurier, Medical Director.

**SASKATCHEWAN**

St. Paul's Hospital, Saskatoon. Sister A. Lachance, Administrator.

This year the College of General Practice has decided that something more might be done to check this unnecessary wastage. Doctors are not expendable. The plan is to have a physical examination of every doctor who attends the Annual Meeting of the College of General Practice in Montreal, March 4-6. To make this plan practical it must be thorough enough to serve as a check on future examinations when a comparison of records is important.

With the limited time, space, and personnel available for this examination we must make it as brief as possible and still make it worthwhile. The following is an outline of this plan:

1. Brief and concise history.
2. X-ray of chest.
3. Electrocardiogram.
4. Blood pressure reading.
5. Haemoglobin and blood sedimentation rate estimations and red cell count.
6. Urinalysis.
7. Weight.

A form will be given to each doctor at the registration desk with a questionnaire on one side which he will be asked to fill in before reporting for the examination. The other side will be left for reports of the various tests. The questionnaire will be as brief as possible to elicit essential information without making it too time-consuming.

The report will be confidential and available only to the doctor concerned. It will be a permanent record for the doctor to retain.

We hope this will be the beginning of a plan to have doctors take better care of themselves and see that they get at least the same care and attention which they extend to their own patients. We are asking for 100% co-operation of doctors attending the convention. The two examination rooms will be arranged so that the examinees will go rapidly from one examination to the next without loss of time.

This is a new venture into the field of preventive medicine for the benefit of the doctors themselves. If it is as successful as we hope, it may be followed at other medical conventions. Canadians are noted for new ideas. Come to the convention prepared to help us put this new one across in a big way.

J. Z. GILLIES, B.A., M.D., *Chairman,*  
Medical Examination Committee.

### HEALTH EXAMINATION OF DOCTORS



EVERY YEAR in every community some doctor dies and the sad news is made worse as the word goes round that he knew for months that there was something radically wrong but just neglected having any examination until it was too late. This has been called to our attention often enough but no one has seen fit to do anything about it.

### CHANGE OF ADDRESS

Subscribers should notify the Canadian Medical Association of their change of address *two* months before the date on which it becomes effective, in order that they may receive the Journal without interruption. The coupon on page 83 is for your convenience.

## Association Notes

### DOMINION INCOME TAX RETURNS BY MEMBERS OF THE MEDICAL PROFESSION

[We publish herewith the text of a memorandum approved by the Department of National Revenue for the guidance of doctors making income tax returns relative to the year 1956.]

As a matter of guidance to the medical profession and to bring about a greater uniformity in the data to be furnished to the Taxation Division of the Department of National Revenue in the annual Income Tax Returns to be filed, the following matters are set out:

Individuals whose income—(a) is derived from carrying on a business or profession (other than farming); (b) is derived from investments; or (c) is more than 25% derived from sources other than salary or wages, are required to pay their estimated tax by quarterly instalments during such year. Each payment must be sent in with Income Tax Instalment Remittance Form T7C. Any balance of Income Tax due is payable on or before the 30th April of the succeeding year, plus interest where applicable.

Doctors who pay salaries or wages to employees are required to deduct tax therefrom in accordance with the Table of Tax Deductions obtainable from District Taxation Offices. Each employee should complete and file one copy of Form TD1 with his employer (a) at commencement of employment and (b) within seven days of any change in circumstances affecting his personal exemptions. If Form TD1 is not filed, tax deductions must be made as though the employee were a single person. Tax deductions withheld from salaries or wages must be sent to the local District Taxation Office not later than the 15th day of the following month accompanied by Tax Deduction Remittance Form TD7A.

The following timetable indicates the returns required:

#### A. Doctors NOT receiving salaries amounting to $\frac{3}{4}$ of income:

Date due	Forms to be used
March 31	Form T7C
April 30	Form T1 General
June 30	Form T7C
September 30	Form T7C
December 31	Form T7C

#### B. Doctors receiving salaries amounting to $\frac{3}{4}$ or more of income:

Date due	Forms to be used
April 30	Form T1 General (Note: Doctors whose earned income consists solely of salary and whose investment income is not over \$2,400 may use Form T1 Short unless they claim a capital cost allowance or a foreign tax credit.)

#### C. Doctors who pay salaries to their own employees:

Date Due	Forms to be used
15th of each month	Form TD7A
February 28	Form T4 Summary and Supplementary.

Details of the total salaries or wages paid to employees and the tax deducted therefrom must be forwarded to the local District Taxation Office on Forms T4 Summary and T4 Supplementary not later than the last day of February in each year.

### INCOME

Under the provisions of the Income Tax Act a doctor is required to maintain an accurate record of all income received both as fees from his profession and by way of investment income. The record should be clear and capable of being readily checked against the return filed. It may be maintained on cards or in books kept for the purpose. Such records must not be destroyed until written permission for their disposal is obtained from the Minister of National Revenue.

### EXPENSES

Under the heading of expenses, the following accounts should be maintained and records supported by vouchers kept available for checking purposes:

- Medical, surgical and like supplies.
- Salaries or wages paid to professional assistants, nurse, office help, bookkeeper. (It is to be noted that the Income Tax Act does not allow as a deduction a salary paid by a husband to a wife or vice versa. Such amount, if paid, is to be added back to the income.)
- Telephone expenses (long-distance charges on business calls and service charges for business telephones listed in the doctor's name, fees for telephone answering services).
- Assistants' fees; the names and addresses of the assistants to whom fees are paid should be furnished. This information is to be given each year on Income Tax form known as Form T4, obtainable from your District Income Tax Office.
- Rentals paid. The name and address of the owner (preferably) or agent of the rented premises should be furnished [see (i)].
- Postage and stationery.
- Depreciation or capital cost allowance as it is referred to in the Income Tax Act; a description of the treatment of depreciation may be found on page 4 of the Income Tax Return Form T1 General under Part XI Method.

The method of computing depreciation for tax purposes is the same as that used last year and you should have no difficulty if you have a copy of last year's return available.

Simply carry forward the balance remaining in each class after deducting last year's allowance. Add to this figure the cost of any new equipment purchased and deduct the proceeds from any disposal of property in each class. The rate you wish to use not exceeding the maximum rate (see below) is applied to this new balance for each class to obtain the depreciation you may claim this year.

The maximum rates for the classes of equipment used by doctors follow:

Capital Item	Class	Annual Maximum Depreciation
Medical equipment		
(a) Instruments costing over \$50 each and medical apparatus of every type .....	8	20%
(b) Instruments under \$50 each ..	12	100%
Office furniture and equipment .....	8	20%
Motor car .....	10	30%
Buildings of frame construction .....	6	10%
Buildings of brick construction .....	3	5%

Where a doctor practises from a house which he owns and resides in, the allowance may be claimed as above on a portion of the cost of the residence, excluding land. For example, if the residence were a brick building costing \$12,000 and one-third of the space were used for the office, the doctor would use \$4,000 as the business portion of the cost and apply the building rate of 5% to determine the maximum depreciation allowable in the first year.



For further information on the subject you may refer to the Income Tax Regulations or you may consult your District Taxation Office.

- (h) Automobile expense (one car). This account will include cost of licence, oil, gasoline, grease, insurance, garage charges and repairs.

The capital cost allowance is restricted to the car used in professional practice and does not apply to cars for personal use.

Only that portion of the total automobile expense incurred in earning the income from the practice may be claimed as an expense and therefore the total expense must be reduced by the portion applicable to your personal use.

- (i) Proportional expenses of doctors practising from their residence

[a] owned by the doctor: where a doctor practises from a house which he owns and as well resides in, a proportionate allowance of house expenses will be given for the study, laboratory, office and waiting room space, on the basis that this space bears to the total space of the residence. The charges cover taxes, light, heat, insurance, repairs, capital cost allowance, and interest on mortgage (name and address of mortgagee to be stated).

[b] rented by the doctor: only the rent and other expenses borne by the doctor such as heat and light will be apportioned inasmuch as the owner takes care of other expenses.

The doctor should be prepared to demonstrate, if called upon to do so, that his apportionment of any particular item is in accordance with the facts relative to that item.

- (j) Sundry expenses. These should cover only small items not otherwise classified, for example, laundry, malpractice insurance, etc. The expenses charged to this account should be capable of analysis and supported by records.

Claims for charitable donations should be made in the space provided for this item on the Income Tax forms and should not be included in the professional expenses. Such claims are allowable as a deduction from income up to 10% of the net income upon submission of receipts to your District Taxation Office.

The annual dues paid to governing bodies under which authority to practise is issued and membership association fees, to be recorded on the return, will be admitted as a charge. Initiation fees and the cost of attending postgraduate courses will not be allowed.

- (k) Interest. Interest paid on borrowed money may or may not be charged as an expense according to the use made of the borrowed money. For example, if it was used to acquire an interest in a partnership or to buy professional equipment, the interest paid may be claimed as an expense in computing professional income, while if it was used to acquire securities or real property, the interest paid may be claimed as an expense in computing the income received from the securities or real property. On the other hand, interest paid on money borrowed for personal use may not be claimed as a deduction from any kind of income.

- (l) Business tax will be allowed as an expense, but Dominion, Provincial or Municipal income tax will not be allowed.

#### CONVENTION EXPENSES

Specific provision for the allowance of convention expenses is made for the first time, in so far as the Income Tax Act is concerned, by Section 3(4) of Chapter 39, Statutes of Canada, 1956, being Section 11(1) (ia) of the Act.

With application to the 1955 and subsequent taxation years, the new paragraph gives authority for the allowance of such expenses to an individual carrying on busi-

ness or practising a profession, but the allowance is restricted to the expense of attending no more than two conventions in a taxation year. Furthermore, if the taxpayer is not a member of the organization sponsoring the convention, his attendance thereat must have been for business or professional reasons. There are no geographical restrictions in the paragraph and the convention, therefore, need not necessarily have been held in Canada for the expenses to be allowable.

As heretofore, the expenses to be allowed must be reasonable, and the taxpayer should show:

- (1) The dates on or between which the convention was held, and the location thereof;
- (2) The number of days he was present at the convention, supported by a certificate of attendance from the sponsoring organization; and
- (3) The expenses incurred, segregating
  - (a) transportation expenses
  - (b) meals, and
  - (c) hotel expenses, for which at least vouchers should be obtained and kept available for inspection.

All expenses of a personal nature, including those attributable to the fact that the taxpayer's wife (or husband as the case may be) accompanied him to the convention, must be excluded from the foregoing.

No expenses for attending a convention are allowable as a deduction from salary income, since such a deduction is prohibited by Section 5 of the Act.

#### PROFESSIONAL MEN UNDER SALARY CONTRACT

The Income Tax Act provides that income from an office or employment is liable to tax without deduction of any kind except such as are specifically provided for in the Act. The allowable deductions include the employee's contributions to a pension fund, alimony, travelling expenses, annual professional membership dues, office rent, salary to an assistant or substitute, and supplies consumed directly in the performance of the duties of employment.

Section 11 (10) (a) of the Income Tax Act permits the deduction from income of an office or employment of annual professional membership dues only if their payment was "necessary to maintain a professional status recognized by statute" and if their payment was "required by (the) contract of employment".

The annual registration fee of the Provincial medical licensing authority would be allowable if paid by the doctor himself.

Certain conditions are attached to the allowance of the expenses, and without trying to recite the exact provisions of the law, the main points are that:

- (a) The expenses must have been incurred in the performance of the duties of the office or employment.
- (b) The employee is required, under the contract of employment, to pay the expenses.
- (c) To claim travelling expenses the employee must be ordinarily required to carry on the duties of his employment away from his employer's place of business. Travelling between the doctor's home and his office is not included.

Where travelling expenses are allowable under these provisions, depreciation may be claimed on the automobile used for this purpose, but no other claim for depreciation may be made.

#### INCOME FROM A PARTNERSHIP

Additional expenses incurred by a partner, but not charged to the partnership, may be claimed as a deduction from the partner's share of income. However, the partner must be in a position to substantiate these expenses, to show why they were not charged directly to the partnership and that they were necessarily laid out to earn the partnership income.

## TRANS-CANADA MEDICAL PLANS

### *Employee Welfare Plan for Non-Operating Employees of the Canadian Railroads.*

After several months of negotiation, the Canadian railway companies and the unions representing their non-operating employees have agreed upon a comprehensive health and welfare package for employees and their dependents, scheduled to go into effect January 1, 1957. These are the highlights: (1) Group life insurance, with a coverage of \$500.00 per employee. (2) Weekly indemnity of \$40.00 in case of sickness or non-occupational disease. (3) Basic hospital expense protection for 70 days at standard ward rates. (4) Surgical and medical benefits.

In British Columbia, Alberta and Saskatchewan, where government hospital schemes exist, basic benefits will not include any hospital coverage, but the full amount of money available for health services will be used for comprehensive medical coverage. In British Columbia the services will be underwritten by Medical Services Association; in Alberta by Medical Services (Alberta) Incorporated; and in Saskatchewan by Medical Services Incorporated and Group Medical Services jointly.

In the other provinces, where the amount of money available has to be used for both hospital and medical care, the Blue Cross Plans will underwrite the hospital services, and the surgical and medical benefits in Manitoba will be provided by Manitoba Medical Service; in Ontario by Associated Medical Services Incorporated; in Quebec by Quebec Hospital Service Association; in New Brunswick, Prince Edward Island and Newfoundland by Maritime Hospital Service Association; and in Nova Scotia by Maritime Medical Care Incorporated.

*Medical Services Included under Basic Coverage in the Provinces of British Columbia, Alberta and Saskatchewan—*(a) On a service basis—coverage for surgical operations. (b) Confinements, including prenatal and postnatal care. (c) Treatment of fractures and dislocations. (d) Administration of anaesthesia, including obstetrical and dental anaesthesia in hospital. (e) Office calls, home calls, hospital calls. (f) Consultations and specialists' care. (g) Special diagnostic procedures, such as B.M.R. and electrocardiogram. (h) Laboratory services. (j) Diagnostic x-ray services. (k) Reimbursement for special nursing services in hospital when ordered by attending physician, on the basis of 75% for the first 7 days and 50% thereafter.

In the provinces east of Saskatchewan, basic coverage benefits for medical services include: (a) Surgical operations. (b) Confinements, including prenatal and postnatal care. (c) Treatment of fractures and dislocations.

Because of lack of available funds in the welfare package to purchase greater hospital and medical benefits, arrangements were made by which the employee (provided the required enrolment percentages are met) may voluntarily purchase additional coverage, on a payroll-deduction basis. Under this arrangement two options are provided.

*Option 1* provides, in addition to the basic package: (a) anaesthesia benefits; (b) diagnostic x-ray services in a doctor's office for suspected fractures and dislocations, up to \$25.00 per person in any 12 months; (c) in-hospital medical care to a maximum of 70 days per illness; (d) consultations by specialists for in-hospital medical treatment cases.

*Option 2* is a further extension of the basic package plus *Option 1*, to include doctors' services in the home and office as well as in the hospital plus the following: Consultations, in or out of hospital; special diagnostic procedures, such as B.M.R., E.C.G.; diagnostic x-ray services to a maximum of \$35.00 per person for any one period of 12 months; laboratory services; x-ray and

radium therapy to a maximum of \$150.00 per person in any 12-month period.

In addition to these, in such provinces as Manitoba, Ontario and Nova Scotia, refractions and well baby care are also included.

Negotiating this contract meant that many other private arrangements then in existence had to be meshed into the new contract so that the employees covered under such schemes were not left unprotected.

Consideration also had to be given to pensioners, and the arrangements provide that present pensioners under coverage among other private schemes now being wound up, and future persons retiring, will be given the opportunity of subscribing to the type of contract currently being offered retirees by the Plan with which the subscriber is enrolled at the rate in force for such type of contract.

Also, employees leaving their position with the railway may, on leaving the group, be given the opportunity of subscribing to the type of "left employ" or "direct pay" contract currently offered by the Plan with which the subscriber is enrolled at the rates in force for such direct pay contract.

All non-operating employees covered under the master agreement who on December 31, 1956, had completed 60 calendar days of service, were covered as of January 1, 1957. New employees eligible for coverage after that date will be covered on the 1st of the month following completion of 60 calendar days. Coverage will also include dependent children under 19 years of age.

There are no waiting periods for pre-existing conditions or maternity benefits.

The medical and hospital phases of the welfare package were negotiated by Trans-Canada Medical Plans and the Canadian Council of Blue Cross Plans, and the group life and weekly indemnity were negotiated by a syndicate of Canadian life insurance companies.

The master agreement specifies that \$4.25 a month be deducted from each employee's pay. This amount will be matched by an equal contribution from the employer. The contract is of 2 years' duration.

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## THE OSLER SCHOLARS

Among the lesser known activities of The Association is that of custodian of The Canadian Medical Association Osler Scholarship Fund. In 1929 seven public-spirited citizens of Montreal contributed a total of \$12,000 to establish this fund and directed that, at intervals of three years, the revenue was to be made available for two Osler Scholarships. One candidate is nominated by the Medical Board of the Montreal General Hospital and one by the Faculty of Medicine of McGill University. The scholarship is awarded "in order that such candidate may pursue special studies to advance the knowledge of medicine and to improve the teaching of clinical medicine".

The nominal roll of Osler Scholars since the inception of the award suggests that the selectors have chosen well and that the objectives of the donors have been realized. Dr. Gordon Copping, Dr. Gerald Evans, Dr. John Howlett, Dr. Stuart Townsend, Dr. W. R. Kennedy, Dr. E. M. Worden, Dr. Hamish McIntosh, Dr. Lester McCallum and Dr. J. C. Beck represent the distinguished company to whom these scholarships have been awarded, and there will shortly be added to their numbers, Dr. David Stubbington and Dr. Douglas Kinnear, who are the recipients of these scholarships for 1957. A.D.K.



## MEDICAL SOCIETIES

AMERICAN PSYCHIATRIC  
ASSOCIATION

A divisional meeting of the American Psychiatric Association was held at the Mount Royal Hotel, Montreal, during November 8-11, 1956, and a large attendance was drawn from many parts of Canada and the U.S.

In the opening session, tribute was paid to Kraepelin (1856-1926), whose systematic observation of psychiatric patients in Munich was one of the foundations of modern psychiatry. Dr. Braceland (Hartford), President of the Association, spoke of Kraepelin's attempts at refining psychiatric diagnoses while maintaining an open mind and a flexible approach. Dr. Farrar (Toronto), Editor of the Association's Journal, gave an evocative account of his visit to Kraepelin's clinic and emphasized Kraepelin's single-minded devotion to psychiatric studies.

An academic lecture was given by Dr. Beach (New Haven), who reported experimental studies of sex drives in various laboratory male animals. He noted that exogenous androgens restored normal mounting activity in rats after castration or partial cortical ablation, while lesions in the posteromedial hypothalamus abolished sexual activity without concomitant endocrine dysfunction. The separation of male genital activity into two phases of tumescence, or arousal and ejaculation, made earlier by other observers, seemed justifiable on experimental grounds. Arousal could be conditioned but not ejaculation. It was emphasized that the above observations did not necessarily apply to humans.

Dr. Cantril (Princeton) demonstrated convincingly with a working model that our presumptions modify perception. In his studies with different pictures in a stereoscope, distortion in fusing two pictures usually occurred; the direction of distortion ran towards emphasizing socially acceptable qualities, the degree of distortion being related to the duration of identification with the subject pictured. Results suggested too that psychiatric patients distort the pictures of other persons more so than the image of themselves, when compared with normal controls.

Dr. Fink (Glen Oaks, N.Y.), reporting on a series of 24 depressed patients given ECT, found that the degree of clinical improvement was related to the amount of delta rhythm (EEG), and to the extent of disorientation following intravenous administration of amylobarbitol. He thought that these and other findings supported the conclusion, made previously by others, that improvement with ECT was linked with denial of illness. Dr. Morello (New York) noted that changes in blood pressure accompanying ECT occurred even if muscular movements were abolished by hypothermia, thus suggesting a central effect of ECT. Dr. Tyhurst (Montreal), in opposing the common view that retirement from work has a deleterious effect on health, stated that mortality and morbidity rates were no worse and in many cases lower than the average in studies on a large group of personnel from one company, but Dr. Macleod (Montreal) pointed out that further sampling was needed as the company under consideration had unusually good welfare schemes for employees. Dr. Tyhurst reported that in most cases of retirement due to age there ensued a transient phase of some emotional turmoil, expressed in various ways, which might last up to one year.

A highlight of the meeting was a further report by Dr. Heath (New Orleans) on the testing on non-schizophrenic subjects of a precipitate (Taraxein), obtained from pooled serum of chronic schizophrenic patients. In smaller doses, a clinical picture resembling simple or paranoid schizophrenia resulted, while larger doses evoked a catatonic or hebephrenic type of response. These effects, produced by intravenous injection of the extract (which is probably a protein), lasted up to two hours in control subjects and up to four days in one schizophrenic patient. The potency of the extract was tested by measuring the spike and wave response in the

septal part of the rostral hippocampus in monkeys with depth electrodes implanted: extracts from non-schizophrenics' serum and other substances did not produce this localized effect in monkeys nor a schizophreniform picture in humans. The effect of the precipitate could be repeated in the same subject: in all cases the effect differed from that of lysergic acid in that autonomic changes were not apparent: side-effects were minimal (nausea, vomiting) and occurred only with earlier batches of the preparation. However, there was usually no specificity of response: for example, extract of serum from paranoid schizophrenics did not usually lead to a paranoid type of reaction in the subjects. Dr. Hoffer (Saskatoon) suggested that this protein-like fraction was an enzyme. Confirmation and elucidation of these significant observations is clearly needed.

Results of drug therapy were given by a number of speakers. Dr. Morrison (Houston, Texas) tried promazine hydrochloride (Sparine) on 30 psychiatric patients, with a maximum daily dose of 2 g. (usual daily maintenance dose of 400 mg.) but only six patients remained improved after three months. Complications were serious and consisted in grand mal fits (23% of cases), confusional states, and delayed agranulocytosis. No extrapyramidal syndrome occurred. However, other speakers reported a success rate of about 30%, using smaller doses and on outpatient cases. Dr. Sainz (New York) told of one patient's death following intravenous Sparine: a precipitous fall in blood pressure occurred. Dr. Wilner (Montreal) advocated the use of dimenhydrinate (Gravol or Dramamine) on psychiatric patients in conjunction with supportive psychotherapy. Twenty-nine out of 40 mixed cases were improved, particularly in terms of anxiety symptoms and tension headaches. Amphetamine was sometimes employed in association. Dosage of Gravol never exceeded 200 mg. daily and side-effects on this dosage were negligible. Dr. Rudy (Galesburg, Ill.) tested two new drugs, MER-22 and SKF-5, both related to azacyclonol and acting as cortical stimulants, on deteriorated chronic schizophrenic patients, without success.

The sessions ended with a lighthearted paper by Dr. Bowes (Montreal) about the compulsive hi-fi addict. A public lecture on the psychology of growth was given to a large crowd by Dr. Arnold Gesell (New Haven, Conn.), well known for his studies on child development.

AMERICAN COLLEGE OF  
SURGEONS MEETING IN  
TORONTO

The American College of Surgeons will hold a three-day Sectional Meeting in Toronto from March 25-27 at the Royal York Hotel. Dr. Stuart Gordon, Assistant Professor of Surgery, University of Toronto, is chairman of the Local Committee on Arrangements, and the program will include panel discussions, symposia, scientific papers, motion pictures, and clinics in Toronto teaching hospitals. A wide and varied program of practical value to the surgeon will include a symposium on the care of the patient with multiple injuries, a panel discussion on treatment of peripheral vascular insufficiency, a symposium on the treatment of advanced carcinoma, a panel on amputations, a symposium on what's new in surgery, a panel on bursitis, and also a special program in ophthalmology, planned under the direction of Dr. A. J. Elliott, Professor of Ophthalmology, University of Toronto. The dinner meeting will be held on Tuesday, March 26, with Dr. Angus D. McLachlin of London, Ontario, in the chair. The guest of honour will be the Honourable Mr. Justice J. Keiller MacKay of Toronto, speaking on "Shakespeare and the Learned Professions". Further information from Dr. H. P. Saunders, Associate Director, American College of Surgeons, 40 East Erie Street, Chicago 11, Illinois.

## PUBLIC HEALTH

### OTTAWA NEWSLETTER

(From the Department of National  
Health and Welfare)

### NUTRITION LABORATORY SERVICE

For every case of scurvy diagnosed in Canada there must be many cases of sore joints, ecchymoses, fatigue or resistant anaemia that are related at least in part to a deficiency of ascorbic acid, and yet never get appropriate treatment because of lack of definitive study. Some hospitals and even some Provincial Laboratories do analyze for ascorbic acid in blood or urine, but these services may not be convenient to the rural or other practitioner who is likely to need them. Very rarely can any practitioner have studies done about vitamin A and carotene, which are important to skin and eyes, and provide useful tests in such diseases as steatorrhœas. Similarly, inflammation and dermatoses around the nose, lips, eyes and ears *may* be due to, or aggravated by, a riboflavin deficiency. A urinalysis can give assurance on this point. A prescription for a "vitamin tonic" may be a waste of money without such evidence, and if such treatment is instituted without the evidence of need it may be difficult to get the evidence later. Aside from obvious or hidden deficiency diseases, the nutritional status often affects the course of other diseases or the way they respond to treatment.

Vitamin analyses can be done on the serum from a few drops of blood taken from a finger puncture, or on a few c.c. of urine, both taken under prescribed conditions. With the co-operation of Provincial Laboratories in each province a service has been established whereby any doctor or hospital may submit blood specimens for analysis of vitamin A, carotene and ascorbic acid and urine specimens for thiamine, riboflavin and niacin. Such analyses and others have been carried out for many years in connection with nutrition studies by the Nutrition Division, Department of National Health and Welfare, Ottawa, who are now offering a service free of charge to bridge the gap until such analyses are readily available.

With blood and urine, certain special procedures must be followed. If ascorbic acid (vitamin C) is involved, its extreme lability necessitates freezing of samples, and shipping in dry ice; several Provincial Laboratories have established a service for this purpose. In all cases the necessary directions are readily available in mimeographed form from the Provincial Laboratory. Special forms are also available so that the Nutrition Laboratory in Ottawa can be as helpful as possible with interpretations. In general, these analyses are not pathognomonic but give valuable clues in a variety of cases.

L. BRADLEY PETT, PH.D., M.D.

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### THE TOXIC HAZARD OF PESTICIDES TO MAN

Since the introduction of the new and more hazardous pesticides after the War, there has been continuing concern on the part of health authorities throughout the world with regard to the impact of these substances on public health. It has been widely recognized that the pesticides of the present period are proving highly effective in controlling disease vectors and in their contribution to agricultural production. Nevertheless,

these advantages have to be weighed against actual and potential dangers to man which many such chemicals present because of their inherent toxicity. The subject is complex and not without controversial aspects. Research is being pursued actively and, *ad interim*, vigilance on the part of health authorities is being maintained. The Director-General of WHO recently convened a small study group to explore the position from the expert point of view. The Group met from June 6-13 under the chairmanship of Dr. W. H. Barnes, of the Serum Research Institute, Carshalton, England, well known for his toxicological research on pesticidal chemicals, and included members from England, France, Sweden, U.S.A., Ceylon, India, Switzerland and Canada as well as representatives from the FAO and ILO.

A number of aspects of the pesticide problem have been of particular concern to health authorities in recent years. It has been known that an occupational hazard is associated with exposure to pesticides and protection for workers has been found necessary, with consideration being given to working schedules, protective clothing and medical supervision. This is a continuing problem as new substances appear.

Food and water contamination has also been a matter of concern in many quarters. This has had to be viewed within the perspective of practical aspects of levels of application, harvesting and storage of treated crops, vector control procedures, and basic toxicity characteristics of different chemicals. The resultant picture has been highly complex. The ingenuity of the chemists who have developed the pesticides has to date outpaced the accumulation of information on the toxic effects to biological species other than the insect under attack. This situation has long emphasized the need for accelerated toxicity research and for more rapid assessment of new examples both in the laboratory and in the field.

The clinical problem in respect to pesticides has been two-fold. Study of case material for signs of intoxication due to long-term exposure to low levels has been a widespread need. At the same time specific diagnostic procedures have been limited. The importance of aids to clinical assessment has been stressed by many authorities. Control of hazards by regulations and codes of practice has been effective in many parts of the world but it has become evident that in the conception and administration of such technical regulations and codes, a high level of rationale must be observed. It has been necessary for administrations to be specially staffed and equipped at the technical and clinical level for control of the problem within the limits of current knowledge. These and other current problems which constitute the background of the subject, afforded a wide area of consideration for the WHO Study Group and its efforts in this direction will be of major interest in many countries.

The toxicity of pesticides to man is a subject which bears a special significance for Canada. We are adjacent to the United States in which a considerable proportion of new pesticides are developed. The economy is substantially agricultural and depends upon high-level, top quality productivity for maintaining a competitive position in local sale and export. In such circumstances the use of pesticidal chemicals is widespread and innovations may always be expected. This has been recognized by many health groups throughout the country and the problem has been studied actively. Hence, Canada has been able to contribute substantially to existing knowledge of the toxicity of pesticides to man and will be among the countries of the world most aided by such international study groups as WHO has convened.



## CORRESPONDENCE

## REFUGEE MEDICAL PERSONNEL

To the Editor:

In view of the plight of currently arriving refugee medical personnel, a committee has been organized under the auspices of the Hungarian Relief Fund to make available information and offers of help to the arrivals.

This committee, organized by Montreal physicians of Hungarian extraction, is in contact with the Provincial Colleges, the universities and various hospitals in order to provide the refugees with up-to-date information on licensing procedures and to place as many as possible in jobs where they can start to comply with the licensing requirements of the country immediately.

It is beyond our competence to plead for special favours for these people, but certainly their courageous fight, the loss of their country and their desperate financial situation merits the fullest co-operation of every member of the profession in the effort to relocate those who choose Canada for their home.

We would like to solicit the help of your Journal in bringing the enclosed message to the attention of all Canadian physicians.

MICHAEL KEERI-SZANTO, M.D.,  
for the Committee.

Refugee Medical Personnel  
Clearing Centre,  
Hungarian Relief Fund,  
904 St. Catherine Street W.,  
Montreal, Quebec,  
December 17, 1956.

*Within the next few weeks, scores of doctors will enter Canada from Hungary. These people are for the most part young, and many of them have a postgraduate education. They speak some English and/or French. They are arriving with families, and with only the clothes on their back. Urgent action is needed to place these refugees in positions where use can be made of their professional skill while they comply with the licensing requirements of this country. Can you help? Address enquiries or offers in duplicate (for display in Toronto and Montreal) to REFUGEE MEDICAL PERSONNEL CLEARING CENTRE, Hungarian Relief Fund, 904 St. Catherine St. W., Montreal.*

## ABSTRACTS from current literature

## MEDICINE

## Localized Interlobar Effusion in Heart Failure: Phantom Lung Tumor.

B. H. FEDER AND S. P. WILK: *Dis. Chest*, 30: 289, 1956.

Localized interlobar effusions are relatively rare, but important enough to merit recognition. When a patient in congestive failure has a pulmonary mass, the possibility of interlobar effusion must be considered before submitting the patient to exhausting studies.

The term "phantom lung tumour" is applied to a transudative interlobar fluid collection in congestive heart failure, which disappears spontaneously with compensation and may reappear with each bout of cardiac decompensation. The localization is believed to be due to pleural adhesions. One of the cases described is not consistent with this explanation. Congestive heart

failure is an essential feature. The interlobar collection of fluid almost always occurs on the right side. On a postero-anterior chest film it appears as a dense, well-delineated shadow of variable shape, not infrequently resembling pulmonary tumour. The "tumour" disappears within a few days on digitalization and diuresis, but may recur with subsequent decompensation. The condition seems to be more frequent than is generally believed.

S. J. SHANE

## Some Factors Affecting Isolation of Tubercle Bacilli from Patients Receiving Chemotherapy.

E. L. DUERR AND T. C. BLACK: *Dis. Chest*, 30: 306, 1956.

Sputum specimens from a series of patients receiving chemotherapy were collected under specified conditions and carefully studied to determine factors affecting isolation of tubercle bacilli, as distinct from response to chemotherapy.

The period of collection of specimens affected results, in that more positive cultures were obtained from 24-hour than from 48-hour specimens. Those collected after more than two but less than six months of chemotherapy showed significant suppression of growth from some specimens; this was not seen from specimens collected after longer periods of treatment.

The drug susceptibility of the organisms appeared to affect results: streptomycin-resistant and PAS-resistant organisms showed little or no suppression; isoniazid-resistant organisms showed some effect, and organisms completely susceptible to all three drugs were most markedly affected.

The particular drugs being currently administered showed a definite effect: PAS had the most marked suppressive action, isoniazid some, but less, and streptomycin little or none under the conditions tested.

S. J. SHANE

## SURGERY

## Inborn and Extrinsic Factors in the Etiology of Peptic Ulcer.

C. F. W. ILLINGWORTH: *J. Roy. Coll. Surgeons, Edinburgh*, 2: 14, 1956.

Both extraneous and intrinsic factors are important in the etiology of peptic ulcer. There is an ulcer type: lean, anxious, alert. Those who have an ulcer, especially a stomal ulcer, are more frequently of Group O blood type than the rest of the population. There is a four-fold predominance of males, and when ulcer occurs in a woman it abates during pregnancy and becomes aggravated at the menopause. Rare in childhood, symptoms suddenly appear in late adolescence. There is a familial and an undeniable geographical incidence.

Among physiological factors are those of acid secretion and mucosal resistance. The acid secretion in duodenal ulcer is high and in gastric ulcer is low. Duodenal mucosa is very resistant, and susceptibility to acid erosion increases the farther away from the duodenum. Trauma and scarring increase the tendency to ulceration. The acid-secreting parietal cells each function on an all-or-none basis, so that hyperchlorhydria is due to a greater number of cells secreting rather than an increased output by individual cells. The duodenal ulcer patient apparently has twice the normal number of parietal cells in his stomach wall.

Mental stress, either an acute incidence of nervous apprehension or long-sustained worry and responsibility, is generally assumed to act by vagus stimulation causing acid secretion. But vagus stimulation also increases muscle tone and activity and this is also a factor in ulcer formation. Cortisone has also been observed to increase ulcer symptoms, increasing acid secretion as well as slowing the repair process.

BURNS PLEWES

### The Early Management of Burns.

W. H. AMSPACHER: *S. Clin. North America*, 1385, 1956.

The author, who was formerly director of the surgical research unit at Brooke Army Hospital and conducted extensive clinical trials on the use of dextran amongst battle casualties in Korea, reviews some practical considerations in therapy of burns. These are of importance to every doctor in this day and age.

Emphasis is of course placed on careful observation and control of fluid and electrolyte balance with use of the indwelling catheter aiming at an output of 30-50 c.c. per hour in the adult. He suggests a modification of the original Evans formula which is probably easier for the average physician. This calls for 1 c.c. of colloid or electrolyte solution per pound of body-weight for each percent of the body which has been burned. Each case must be individualized but as a rule 30 to 40% of the solution is colloid. Deeper burns require whole blood.

Burn trauma to the respiratory tract is considered to be rarely the result of the heat *per se* but caused by the inhalation of noxious gases thrown off by combustion of certain materials. They are more common in persons burned within a closed space.

It is an accepted fact that even severely burned patients stand travel better in the early stages, after resuscitation therapy, rather than later. The reader is reminded of the importance of tetanus antitoxin or toxoid administration in addition to ordinary antibiotic coverage. Tracheotomy is often imperative in burns of the face.

ALLAN M. DAVIDSON

### ORTHOPÆDICS

#### Fracture of the Spine.

M. B. HOWORTH: *Am. J. Surg.*, 92: 573, 1956.

This article is a concise yet quite comprehensive review of the types, etiology, pathology, clinical and roentgenological features and treatment of various spinal fractures. Forty representative radiographs and diagrams are used to illustrate salient features of this injury, in which early recognition and proper therapy are of paramount importance.

The reader is reminded of the associated injuries that may occur to ligaments, intervertebral discs, spinal cord, nerve roots and other soft tissues in addition to the various vertebral components. Moderate or severe wedging is often associated with forward subluxation, tearing the interspinous ligament. This injury, especially if associated with fracture or dislocation of the articular facet, is a potential threat to nerve or cord damage because of primary compression or instability.

Reference is made to the importance of various x-ray views such as oblique, spot and stereoscopic in addition to the ordinary anteroposterior and lateral projections. Attention must be paid to positioning for accurate definition of disc spaces, pedicles and articular processes. It has been stated that exposing the posterior portion of the spine for fusion reveals associated fractures of the posterior elements in 15% of cases. Many of these are unrecognized because of the difficulty in demonstrating them roentgenographically. Compression of both superior and inferior surfaces without comminution, often without wedging in the early stages, is usually indicative of involvement in metastatic tumour. An interesting radiograph is presented to show the characteristic destructive lesion of advanced tuberculosis of the spine with marked wedging of one lumbar vertebra and almost complete disappearance of the body of the one below due to bone absorption.

In dealing with congenital deformities the author refers to the present consensus that the basic defect between the superior and the inferior articular facets is developmental. Although trauma may increase the displacement, it is "not a fracture but a separation, probably on a nutritional basis".

After stating that hyperextension as usually practised is not effective in producing real correction of the compression, he warns of the dangers and advises against these methods if there is damage to the spinal cord, dislocation of the lateral articulations or fracture of the neural arch. The indications for and disadvantages of plaster immobilization and use of the Taylor splint are discussed. A plea is also made for early fusion in younger males; especially those whose back must withstand a fairly rigorous routine. Fractures of the posterior elements especially require more protection. In this type the results of either operative or conservative therapy are less satisfactory. On the other hand, those in whom fusion was done for compression fracture had good symptomatic and functional results in 92% of cases.

ALLAN M. DAVIDSON

### DERMATOLOGY

#### Sensitization Dermatitis to Carrots.

J. V. KLAUDER AND J. M. KIMMICH: *A.M.A. Arch. Dermat. & Syph.*, 74: 149, 1956.

The authors report 13 cases of contact dermatitis on the hands and forearms caused by carrots. These cases occurred in a canning factory. The incubation period was usually about two weeks. Patch tests to unpeeled raw carrot were positive in all cases. Improvement was rapid after exposure was stopped. There was no reaction from eating carrots in any of these cases, apart from oedema of the lips and perioral dermatitis in one patient. Three patients also had positive patch tests to other botanically related vegetables such as parsnip, turnip-rooted celery, and Pascal celery. The degree or duration of exposure to these vegetables by the ordinary housewife is probably not sufficient to cause sensitization.

ROBERT JACKSON

#### Diagnosis of Foot Ringworm.

J. G. HOLMES AND J. C. GENTLES: *Lancet*, 2: 62, 1956.

Two thousand men were selected at random from collieries and power stations and examined clinically and mycologically for foot ringworm. Correlations between clinical findings and laboratory findings are reported in some detail. Vesiculation and erythema were the two most valuable signs, whereas maceration and peeling were found to be unreliable. Foot ringworm should be diagnosed only when clinical symptoms can be supported by culture of a pathogenic fungus or its microscopic demonstration in skin scrapings. In the vast majority of cases, two negative laboratory reports will exclude the disease. The response to treatment by antifungal preparations is no criterion for diagnosis.

ROBERT JACKSON

### THERAPEUTICS

#### Observations on Treatment of Tuberculous Meningitis with Saluzid.

A. L. BERNSTEIN, P. B. KRASILSHIK AND A. A. SHELAGUROVA: *Klinitsheskaya Meditsina*, 34: No. 7, 55, 1956.

Saluzid is a new drug synthesized by Russian chemists. It belongs to the group of hydrazones of isonicotinic acid (formula not given) and is administered orally or injected subarachnoidally as a 5% solution. The authors report their observations on 55 patients with tuberculous meningitis treated with saluzid. The patients were divided into two groups: (1) treated with saluzid only; (2) treated with saluzid plus streptomycin. The first group (10 patients) received daily oral doses of 0.75-1.5 g. and daily injections of 1-3 ml. of the drug solution. In cases of acute meningitis (four patients) the



results were negative and the treatment was discontinued. Favourable results were observed in cases of recurrent meningitis (six patients) treated with saluzid only. In the second group 31 patients underwent alternating courses of treatment with streptomycin and saluzid with good results. Best results, however, were obtained in 14 patients who were treated with both drugs simultaneously, i.e. alternating subarachnoid injections plus intramuscular injections of streptomycin and oral administration of saluzid. After a treatment period of 200-240 days no toxic effects were apparent.

V. R. JABLOKOW

#### Arlidin.

I. D. STEIN: *Ann. Int. Med.*, 45: 185, 1956.

Two hundred and twenty patients with intermittent claudication as the chief manifestation of a deficient blood supply to the working muscles of a limb were treated with a recently introduced vasodilator drug, Arlidin. Their vascular insufficiency arose from organic arterial disease. It resulted in acute symptoms in 21 patients, and slow development and gradual progression of symptoms in 199 patients. It was in this last-mentioned group that the commonly used vasodilator drugs had little value in increasing walking tolerance, after the initial salutary effect seen from the initial use of most new drugs. In contrast, when placed on oral Arlidin, two-thirds of these "stabilized" patients had a significant increase in ability to walk. Intra-arterial injection of a single 6-mg. dose resulted in an average increase of blood-flow in the calf of 300 to 400%. Arlidin is an effective dilator of blood vessels in skeletal muscle and should be used in the management of the omnipresent symptom, intermittent claudication.

S. J. SHANE

#### Use of Anti-Rheumatic Drugs in Prophylaxis of Acute Rheumatism.

M. A. YASINOVSKII *et al.*: *Klinicheskaia Meditsina*, 34: No. 6, 31, 1956.

Rheumatic fever is regarded as a chronic disease which becomes periodically acute. According to the data collected in the authors' clinic, among approximately 160 patients suffering from acute rheumatism the factors which brought about exacerbation of the disease were in 30% of cases tonsillitis, 15.8%—influenza, 25%—pneumonia; the rest were various other infections and traumatic causes. Tonsillectomy is indicated in certain cases of recurrent acute rheumatism. The most important step in the prophylaxis of acute rheumatism is a timely prevention of streptococcal infection of the upper respiratory tract. For this purpose penicillin and "bicillin" have been used widely with good results. The authors point out that very prolonged administration of penicillin is not without disadvantages; on the other hand, antibiotics and even sulfanilamide preparations may bring effective results if administered in large doses over a period of only 7-10 days. Against rheumatism as an allergic disease such desensitizing drugs as sodium salicylate, "analgin" and particularly pyridone have been used effectively by Yasinovskii for over 20 years as a means of preventing recurrence of the disease. The authors suggest that active anti-rheumatic drugs should preferably be used over short periods of time when the danger of recurrence is acute, as after upper respiratory infections or after surgical interventions or other trauma. The action of these drugs is both anti-allergic and anti-inflammatory. The authors report that out of 200 rheumatic patients who were kept under observation while they received the treatment with anti-rheumatic drugs (1½ to 3 years) only 7 persons (3.5%) suffered an acute exacerbation. This result is significant in view of the fact that normally over 50% of rheumatic patients suffer recurrence of the disease within three years of the first attack.

V. R. JABLOKOW

## OBITUARIES

DR. GEORGE VICTOR BURTON, 55, died in the Yarmouth Hospital, N.S., on November 29. He graduated from Harvard University Medical School in 1924. Dr. Burton served as a general practitioner, specializing in surgery, in Yarmouth. He was Chief of Surgery of the Yarmouth Hospital.

He is survived by his widow.

DR. ANDREW P. DAVIES, 68, died in hospital in Ottawa on November 25. He graduated from McGill University. Dr. Davies served overseas during World War I and practised in Ottawa. He was club physician for the Ottawa Football Club.

Dr. Davies is survived by his widow, three sons and two daughters.

DR. MORRIS KINSEY DILLANE, 82, a physician at Schomberg, Ont., for over 50 years, died in St. Michael's Hospital, Toronto, on December 1. He was born in Tottenham, Ont., and graduated from the University of Toronto in 1899. Dr. Dillane began practising in Schomberg in January 1900. He was chairman of the Schomberg Red Cross in World War I and was Medical Officer of Health for King township for many years.

He is survived by his widow, three sons and a daughter.

DR. H. F. DONAHUE, 72, a founder of the Newfoundland Medical Association and the Newfoundland Division of the Canadian Medical Association, died in St. John's on December 2. He was born in New York City, and graduated from McGill University, Montreal, in 1909. Dr. Donahue practised at Grand Falls, Norris Arm, Fogo and Torbay, Nfld. He moved to St. John's in 1924.

He is survived by one son and two daughters.

DR. JEAN B. GAGNON, 63, a lung specialist, died on November 28 in Montreal. He was born in St. Jean, Que., and graduated from Laval University in 1920. He did postgraduate work in lung diseases in the hospitals of Paris, France.

Dr. Gagnon is survived by his widow.

DR. JACOB GOLDSTEIN, 50, senior attending obstetrician and gynaecologist at New Mount Sinai Hospital, Toronto, died on January 1. He was born in Toronto, and graduated from the University of Toronto in 1930. Dr. Goldstein did postgraduate work in New York, Cincinnati, Chicago and Jersey City, and began to practise in Toronto in 1936. He was a Fellow of the Society of Obstetricians and Gynecologists of Canada, the American College of Obstetricians and Gynecologists, and the International College of Surgeons. He was a licentiate of the Royal College of Physicians and Surgeons of Canada.

Dr. Goldstein is survived by his widow and three daughters.

DR. E. P. KELLY, 58, chief surgeon of the Notre Dame Hospital in Hawkesbury, Ont., died at his home on December 1. He was born in Buckingham, Que., and graduated from McGill University. He was licensed by the Royal College of Physicians and Surgeons in Edinburgh, specialized in surgery at Vienna, and practised medicine in London, England, for one year. Dr. Kelly practised for 30 years in Hawkesbury, where he had established his own hospital in 1927.

He is survived by his widow, two sons and two daughters.

DR. DUNCAN McCALLUM, head of the Eastern Division Chest Clinic for the Ontario Department of

Health, died in Ottawa on December 2. He was born in King, Ont., and graduated from the University of Toronto in 1918. Dr. McCallum specialized in tuberculosis for two years at the Muskoka Sanatorium and was at one time on the staff of the Christie Street Hospital, Toronto.

DR. GEORGE HERBERT MANCHESTER, 85, died in New Westminster, B.C., in November. He was born in Ottawa, and graduated from McGill University in 1894. Dr. Manchester did postgraduate work in England. He served as house surgeon at the Montreal General Hospital, and afterwards became medical superintendent at the Verdun, Que., Mental Hospital, and medical superintendent of the New Westminster Mental Hospital. During World War I he was psychiatrist to the Third Imperial Army in France. He was appointed to the Canadian Pensions Board, and served on the staff of Shaughnessy Hospital in Vancouver for eight years, before returning to New Westminster.

DR. H. HERBERT MURRAY, a practitioner in Toronto for many years, died at his home on December 2. He was born in Mitchell, Ont., and graduated from the University of Toronto in 1910.

Dr. Murray is survived by his widow.

DR. DAVID PERLMAN, 63, chief anaesthetist at New Mount Sinai Hospital, Toronto, died there on December 10. He was born in Toronto, and graduated from the University of Toronto in 1918. Dr. Perlman was a captain in the Royal Canadian Army Medical Corps before he began to practise in Toronto.

He is survived by his widow and two daughters.

DR. ARTHUR JOSEPH PRENTICE, 76, died on December 18 in Toronto. He was born at Drumbo, Ont., and graduated from the University of Toronto in 1907. Dr. Prentice was on the staff of St. Joseph's Hospital in Toronto for 25 years, and later at the Northwestern General Hospital, which he helped to organize.

He is survived by his widow, one daughter and a son.

DR. HENRI SANSON, 86, a retired medical health officer in the Province of Quebec, died on November 1 at St. Hyacinthe, Que. He was born at Saint-Allouestre, France, and was admitted to the practice of medicine in Montreal in 1899. He did public health work in Michigan before taking up an appointment in Montreal in 1914.

Dr. Sanson is survived by two sons and one daughter.

DR. FREDERICK TOMINGAS, 62, staff doctor at the Queen Elizabeth Hospital, Toronto, died there on December 27. He was born in Estonia and received his training as a specialist in obstetrics and gynaecology there. Dr. Tomingas came to Canada in 1950 and practised at the Regina General Hospital before going to Toronto.

He is survived by his widow.

DR. OWEN C. TRAINOR, 62, died in his office in the Parliament Buildings, Ottawa, on the morning of November 28, while the House was in session. The Prime Minister announced the news to members and adjourned the debate till 8.00 p.m. Born at Moncton, N.B., Dr. Trainor was educated at St. Dunstan's, Charlottetown, P.E.I., and at McGill University, graduating in medicine in 1920. He registered in Manitoba in 1922 and after two or three years spent in the Pathology Department of the Winnipeg General Hospital he became pathologist and director of Misericordia Hospital, Winnipeg. A few years ago he opened a laboratory for clinical pathology. He was certified as a

specialist in pathology by the Royal College of Physicians and Surgeons of Canada. In 1938 he was president of the Winnipeg Medical Society and in 1951 president of the Canadian Hospital Association. He was keenly interested in the Manitoba Hospital Service Association. In 1953 he was elected to represent South Winnipeg in the House of Commons as a Progressive Conservative.

He is survived by his widow and one son, John Michael, who is a doctor in New York.

#### OWEN C. TRAINOR, M.P.

##### AN APPRECIATION

Death laid his hand on Dr. Owen C. Trainor, M.P. for Winnipeg South, in his office in the Parliament Buildings on the morning of November 28. The House was in session. When the news reached the Prime Minister he rose and, in a voice choked with emotion, moved adjournment of the debate until evening. The Hon. Stuart Garson, Minister of Justice, Mr. Earl Rowe, M.P., leader of the Opposition, and Mr. Stanley Knowles, M.P. for Winnipeg Centre, spoke of the qualities which had endeared the late member to the House.

Owen Trainor may justly be claimed to be a martyr to public duty. Earlier in the year during the heat of the pipeline debate he suffered a heart attack which necessitated a stay in an Ottawa hospital. He was advised not to return for the present session but the urgency of the Middle East situation compelled him to take his seat.

In 1953, with no previous political experience, he won back for the Progressive Conservative party a seat which had been held by the previous Liberal member for 18 years. He soon became a spokesman for his party on medical questions. The special knowledge of hospital affairs acquired through long years as director of Misericordia Hospital, Winnipeg, and as a member of the Manitoba and Canadian Hospital Associations and the Manitoba Hospital Service Association, enabled him to speak with authority on the subject of a national health scheme. He opposed compulsory national health insurance and favoured voluntary hospital and medical prepayment plans. His quiet sincerity and conciseness made him an effective speaker in the House. Had he lived and had there been a change of government, he might have been the next Minister of Public Health and Welfare. At 62 he was still in the plenitude of his mental powers.

His medical colleagues in Winnipeg held him in like high regard. Both in the hospital and in the clinical field he was a capable pathologist. In 1938 he was elected President of the Winnipeg Medical Society and in 1951 he was President of the Canadian Hospital Association.

One might differ with Owen Trainor without ceasing to respect and even admire him for his gentleness, his knowledge and his lack of ostentation. One might say of him as Milton of Lycidas: "How well could I have spared for thee."

Our sympathy goes out to his widow and his son, Dr. John Michael Trainor of New York. R.M.

DR. EDWARD G. VERNON, 71, died at his home in Clarkson, Ont., on November 20. He was born in St. Mary's, Ont., and graduated from the University of Toronto in 1910. He practised for three years in Cochrane, Ont., before moving to Clarkson in 1915.

Dr. Vernon is survived by his widow and two sons.

#### SIR LIONEL WHITBY

Lady Whitby and family desire to express their warmest thanks to the many friends and colleagues of the late Sir Lionel Whitby who so kindly sent messages of sympathy and condolence in the loss they have sustained.



## FORTHCOMING MEETINGS

## CANADA

COLLEGE OF GENERAL PRACTICE OF CANADA, First Annual Scientific Convention, Montreal, Quebec. (Dr. J. Y. Tremblay, 3244 Beaubien, Montreal, Que.) March 4-6, 1957.

CANADIAN SOCIETY OF MICROBIOLOGISTS, Annual Meeting, London, Ontario. (Professor J. A. Carpenter, Department of Bacteriology, Ontario Agricultural College, Guelph, Ont.) June 10-12, 1957.

CANADIAN MEDICAL ASSOCIATION, 90th Annual Meeting, Edmonton, Alberta. (Dr. A. D. Kelly, General Secretary, 150 St. George Street, Toronto 5, Ontario.) June 17-21, 1957.

CANADIAN OTOLARYNGOLOGICAL SOCIETY (SOCIÉTÉ CANADIENNE D'OTOLARYNGOLOGIE), Annual Meeting, Banff Springs Hotel, Banff, Alta. (Dr. G. A. Henry, Secretary, 328 Medical Arts Bldg., Toronto, Ont.) June 17-19, 1957.

NINTH INTERNATIONAL CONGRESS OF RHEUMATIC DISEASES, Toronto, Ontario. (Ninth International Congress of Rheumatic Diseases, P.O. Box 237, Terminal "A", Toronto, Ont.) June 23-28, 1957.

## UNITED STATES

FIRST MEDICAL MOTION PICTURE WORKSHOP, Kansas City, Missouri. (The Calvin Company, Inc., 1105 Truman Road, Kansas City 6.) February 4-6, 1957.

INTERNATIONAL ANÆSTHESIA RESEARCH SOCIETY, Phoenix, Arizona. (Dr. A. William Friend, 13951 Terrace Road, Cleveland 12, Ohio.) April 1-4, 1957.

PAN AMERICAN ASSOCIATION OF OPHTHALMOLOGY, Fourth Interim Congress, in conjunction with National Society for the Prevention of Blindness, New York, N.Y. (Dr. Frank H. Constantine, 30 West 59th Street, New York 19, New York.) April 7-10, 1957.

FIRST PAN AMERICAN CANCER CYTOLOGY CONGRESS, Miami, Florida. (Dr. J. Ernest Ayre, 1155 N.W. 14th Street, Miami, Florida; or Mrs. Elizabeth Maselli, Corresponding Secretary, P.O. Box 633, Coral Gables, Florida.) April 25-29, 1957.

NATIONAL TUBERCULOSIS ASSOCIATION, Kansas City, Missouri. (National Tuberculosis Association, 1790 Broadway, New York 19, N.Y.) May 6-9, 1957.

## OTHER COUNTRIES

INTERNATIONAL COLLEGE OF SURGEONS, 10th Biennial International Scientific Congress, Mexico, D.F., Mexico. (Dr. Max Thorek, International Secretary General, International College of Surgeons, 850 W. Irving Park Road, Chicago 13, Illinois.) February 24-28, 1957.

ANNUAL HEALTH CONGRESS, Folkstone, Kent, England. (Secretary, Royal Society for the Promotion of Health, 90 Buckingham Palace Road, London, S.W.1, England.) April 30-May 3, 1957.

HARVEY TERCENTENARY CONGRESS 1957, London, England. (Secretariat, Royal College of Surgeons, 11 Chandos Street, Cavendish Square, London, W. 1, England.) June 3-7, 1957.

TENTH INTERNATIONAL HOSPITAL CONGRESS, Lisbon, Portugal. (Captain J. E. Stone, Secretary General, 10 Old Jewry, London, E.C. 2, England.) June 3-7, 1957.

FIFTH INTERNATIONAL CONGRESS OF THERAPEUTICS, Utrecht, Netherlands. (Dr. F. A. Nelemens, Secretary General, Bureau provisoire: Vondellaan 6, Utrecht, Netherlands.) June 5-7, 1957.

TWELFTH INTERNATIONAL CONGRESS ON OCCUPATIONAL HEALTH, Helsinki, Finland. (The Congress, Työterveyslaitos, Haartmaninkatu 1, Helsinki-Töölö, Finland.) July 1-6, 1957.

## PROVINCIAL NEWS

## NOVA SCOTIA

Dr. Ian MacKenzie, consultant in general surgery for the West Cumberland hospitals, England, has been appointed Professor of Surgery at Dalhousie University and head of the Department of Surgery at the Victoria General Hospital. The appointment was announced jointly on November 27 by President A. E. Kerr of Dalhousie University and Gordon S. Cowan, Q.C., M.P., Chairman of the Board of Hospital Commissioners.

Dr. MacKenzie was born on the Island of St. Kilda, Outer Hebrides, 45 years ago, and completed his undergraduate education and graduate work in surgery and pathology at Edinburgh University. Dr. MacKenzie has always been interested in research work. Most of his research has been carried out at Edinburgh University, and he spent one year doing research work on carcinoma in New York City. During World War II, he saw considerable military service in Europe and the Middle East.

Dr. MacKenzie's appointment marks the first time in the history of Dalhousie that the faculty of surgery has had a full-time professor. Dalhousie thereby associates itself with the general trend of full-time professorships across Canada. Dr. MacKenzie will assume his new duties during the spring term. We look forward to his coming with the keenest of interest, and will be glad to welcome him.

Thursday, November 29, was the occasion of the Annual Dinner of the Victoria General Hospital medical staff at the Lord Nelson Hotel. The guests at the head table were the Honourable Richard A. Donahue, the newly appointed Attorney General and Minister of Health, and Gordon S. Cowan, Q.C., M.P., Chairman of the Board of Hospital Commissioners.

Dr. Judson V. Graham was honoured at this dinner on the occasion of his retirement from the active staff of the Victoria General Hospital. Dr. Harry O'Brien expressed the appreciation and best wishes of the staff of the Victoria General Hospital; to this Dr. Graham replied in an appropriate manner.

The Federal Minister of Health, the Hon. Paul Martin, has announced that a National Health Grant of more than \$17,000 will go to Nova Scotia on behalf of psychiatric work centred at Digby. The Minister revealed that federal authorities have agreed to provide funds recommended by Nova Scotia for operation of a mental health clinic to serve an estimated 70,000 people in the counties of Yarmouth, Digby and Annapolis. Financial assistance is also being given by the Provincial Government and Cornell University.

Mr. Martin noted that the service will provide psychiatric service to this large area; make possible yearly examinations of all patients in county homes and hospitals not only in Yarmouth, Digby and Annapolis, but also in Shelburne and Queens; and provide a follow-up service for patients discharged from the Nova Scotia Hospital.

At the same time the Minister announced approval of a federal grant of \$8,000 for an addition to the Biochemistry Laboratory of the Victoria General Hospital.

The fourth Maritime Hospital Association Institute meeting was held in the Victoria General Hospital during the past week. This meeting had a large attendance, and a wide variety of subjects pertaining to hospital administration were discussed. One recommendation was that the nurses working the rotation shifts in the afternoon and evening should receive an additional ten dollars a month. It is hoped that this increase will be approved.

Dr. Gordon Fryer of the Department of National Health and Welfare, Ottawa, spoke on the subject of "disaster" planning for all hospitals, large and small. He

referred to the Springhill disaster of a few weeks ago in stressing the importance of hospital preparedness.

Dr. R. M. MacDonald, Assistant Superintendent of the Victoria General Hospital, spoke on the problem of staphylococcus infections in hospitals, the measures required to control this complication should it break out, and the measures which should be taken to prevent its occurrence.

The medical fraternity of Halifax welcomes Dr. James Belmano to our midst. Dr. Belmano is a graduate of Dalhousie University and has spent the last four and one-half years as senior resident in the Boston City Hospital where he was doing postgraduate study in general surgery. Dr. Belmano was recently certified by the Royal College of Surgeons of Canada and will be associated with Dr. John Merritt.

W. K. HOUSE

## QUEBEC

Succeeding the late Dr. Lyman Duff, McGill University has named Dr. Lloyd Grenfell Stevenson the new dean of medicine. Dr. Stevenson came to McGill in 1954 as medical librarian and associate professor in the history of medicine. He now takes the status of full professor together with the deanship, and will continue as medical librarian and assistant librarian of the Osler Library.

Dr. Stevenson, aged 38, was born in Ontario and is a graduate of the University of Western Ontario and Johns Hopkins University, Baltimore. He was the first Markle scholar in history of medicine and began as a lecturer in his specialty in 1946 at the University of Western Ontario. He subsequently was promoted to assistant and then to associate professor there.

As part of its 10th anniversary, the Governor-General, the Rt. Hon. Vincent Massey, officially inaugurated recently a new wing of Dieppe House. This institution which specializes in the care of epileptics is located south-east of Montreal, in nearby St. Hilaire. The Governor-General also unveiled a plaque in memory of the founder of Dieppe House, the late George A. Savoy, and placed a wreath in the main lobby on the memorial to the late Major Paul A. Savoy and all Canadians killed in the Dieppe raid.

During the week of November 4 several hundred psychiatrists and psychoanalysts from Eastern Canada and Northeastern United States attended a four-day regional meeting of the American Psychiatric Association in Montreal. The principal subjects at this meeting were the cause and treatment of mental illness. Dr. Francis Braceland, president of the American Psychiatric Association, paid particular tribute in his presentation to Dr. Emile Kraepelin of Heidelberg upon whose work the foundation of much of today's modern psychiatry was built. He stressed that when mental illness began to be studied scientifically, the disgrace of mental disease began to lift and modern methods of diagnosis and treatment were established.

Early in November Professor G. F. Marrian of the department of biochemistry, University of Edinburgh, addressed the first regular meeting of the Montreal Medico-Chirurgical Society for the session 1956-57. He spoke on the endocrine approach to cancer, based on extensive investigations by his group on patients with advanced metastatic breast cancer. These studies combined clinical and radiological assessment with the most complete laboratory assessment yet done in such patients. Urinary excretions of oestrogens, pregnanediol, ketosteroids and gonadotrophins were measured before, during and after successive treatments with stilboestrol, testosterone propionate, ACTH and by adrenalectomy. Although no particularly startling data were secured,

the results have suggested several new endocrine approaches in the study of this disease.

The second regular meeting of the Society was held on November 16, at which Dr. Edward A. Bartram, assistant professor of medicine at the University of Western Ontario, presented an excellent review of the management of coronary heart disease.

During the month of November the postgraduate teaching staff of the Royal Victoria Hospital in Montreal conducted a very successful refresher course for general practitioners. A full quota of applicants from near and far attended.

During the weekend of December 1 and 2, the Montreal Children's Hospital moved to its new buildings at Atwater and Dorchester Streets. Some 100 patients, ranging from infants to 16 years in age, were transferred from the present buildings on Cedar Avenue. This move raised the bed capacity from 175 to 385. The new buildings occupy the old Western division of the Montreal General Hospital and a new 13-storey Atholstan wing named for the late Lord Atholstan, an outstanding past benefactor of the hospital. Also included is a new residence for student nurses on Essex Street across from the hospital.

For the present only 235 beds will be opened, with the others being made available in response to demand. In the new buildings patients will be segregated according to sex, age and disease groups, and private and semi-private rooms will be available. The largest ward takes six children. The age limit has been raised to 16 and 17 in order to accommodate these with their own age groups rather than with adult patients. The hospital now will also welcome mothers living in with their young patients and adequate waiting-room accommodation is available. The outpatient service now located on St. Antoine Street will be transferred to the new buildings.

Cost of the new buildings, totalling \$10,786,311, includes \$2,250,000 paid to the General for the Western division. Much of this money was raised in three recent Joint Hospital Fund campaigns.

Rehabilitation and reasonable teaching facilities are now available. Research space has been planned and will be added as funds become available.

A. H. NEUFELD

## MANITOBA

Dr. M. R. Elliott, Deputy Minister of Health and Welfare for Manitoba, was elected vice-president of the American Public Health Association at its 84th annual meeting in Atlantic City, N.J.

His many Manitoba friends will be pleased to hear that Dr. F. W. Jackson, who recently retired as director of health services, federal Department of Health and Welfare, has been awarded the Sedgwick memorial medal for distinguished service in public health by the American Public Health Association. Dr. Jackson practised at Wawanesa and later was Deputy Minister of Health and Public Welfare of Manitoba and secretary of the Manitoba Medical Association. He is the first Canadian to receive the Sedgwick medal.

Dr. Jack Mendelson has opened an office for the practice of ophthalmology and ophthalmic surgery at 203 Boyd Building, Winnipeg.

Dr. Thomas K. Goodhand and Dr. W. E. Abbott, University of Manitoba, have been awarded grants of \$1085 each for physiological research, and Dr. John T. MacDougall, University of Manitoba surgical research laboratory, a grant of \$500 from the Banting Research Foundation.



The Manitoba Medico-Legal Society met at the Medical College on Nov. 20. There was an open forum on the subject of "Sudden Death", the speakers being Dr. R. E. Beamish, Dr. H. M. Ross, Dr. Athol Gordon and Mr. Charles Huband.

Approximately 16,000 Manitoba railway men and 24,000 dependents will be covered by the employee benefit plan negotiated in Montreal by the unions, railway management, Blue Cross, Manitoba Medical Service and insurance companies.

The new Children's Hospital was formally opened by the Hon. J. S. McDiarmid, Lieutenant-Governor of Manitoba, on the afternoon of Dec. 2. Dr. F. G. Robertson, M.P., parliamentary assistant to the National Health Minister, delivered the opening address. The Hon. R. W. Bend, Manitoba Minister of Health and Welfare, also spoke. On the evening of Dec. 3 the new doctors' lounge was opened in the presence of more than 200 doctors and their wives. The library of the lounge is dedicated to Dr. Bruce Chown. Dr. Harry Medovy spoke of Dr. Chown's work which has brought both national and international attention to the Children's Hospital. Other speakers were Dr. Wallace Grant, president of the medical staff, Dr. Colin Ferguson, chief surgeon, and Mrs. A. M. Oswald, president of the Hospital Board.

ROSS MITCHELL

## ALBERTA

Chief topics of discussion at the recent annual meeting of the Association of Alberta Hospitals were the need for hospitalization facilities for chronic cases and the revised provincial hospitalization plan.

With the active treatment hospitals overcrowded and the old folks' homes not open to bedridden patients, the need for hospitals for chronic cases is acute. Resolutions requested an immediate assessment of the situation by the provincial government and an early start on the construction of needed units.

The proposed hospitalization plan would cover all residents of Alberta and supply standard ward care as well as diagnostic and treatment services. The cost to the patient would vary from \$1.50 to \$2.00, depending on the size of the hospital, the remainder of the cost being split between the municipality and the provincial government; this arrangement could be fitted into the proposed Dominion-provincial plan when the latter becomes a reality.

Representatives of the government have discussed the plan with representatives of the various interested organizations, doctors, nurses and municipalities. Further discussions are planned in an effort to satisfy all parties before the scheme goes into operation, probably in April or July.

Curling has become a major sport among doctors in Alberta and elsewhere in the West to the extent that in April rocks will be thrown in Edmonton in the first inter-provincial doctors' bonspiel between Alberta and Saskatchewan.

The movement started in Edmonton in 1947 with two rinks of doctors curling each Saturday. Today the Saturday group numbers 14 rinks while a second group who curl on Wednesdays is made up of six. Keen rivalry exists between those who have different days of leisure and in 1949 the Hudson's Bay Company put up a trophy for the winner of the Saturday-Wednesday play-off. The cup, known as the McDoctor's Briar, is presented at the annual banquet which winds up the season. Last year 100 curling doctors and their wives attended the banquet, at which it has become traditional for the wives and doctors to stage the entertainment on alternate years.

The other centres for doctors' curling are Calgary with 14 rinks and Lethbridge with six. In 1950, Dr. J. M. Lees of Edmonton and Dr. W. E. Ingram, Calgary, got

together and organized a North-South doctors' bonspiel which the next year became the Alberta doctors' bonspiel, open to all rinks of doctors who wish to compete. The venue is variously Edmonton, Calgary and Lethbridge where the four trophies are competed for in four daytime competitions while the evenings are devoted to fellowship and entertainment which brings the doctors of the province and their wives into pleasant communion.

The presence of 24 rinks from various parts of the province in Edmonton in November of 1956 indicates the enthusiasm with which this recreational activity is received. Hopes are expressed that the Alberta-Saskatchewan bonspiel is merely a beginning and that later competitions will include representatives from other provinces.

W. B. PARSONS

## CANADIAN ARMED FORCES

A meeting of the Canadian Forces Medical Council chaired by Dr. J. A. MacFarlane, Dean of Medicine, University of Toronto, was held in Toronto on December 10. The meeting was attended by: Dr. MacFarlane; Brigadier K. A. Hunter, Coordinator of Medical Services; Dr. G. E. Hall, President and Vice-Chancellor, University of Western Ontario; Dr. R. Lemieux, President, Canadian Medical Association; Dr. J. W. Macleod, Dean of Medicine, University of Saskatchewan; Surgeon Commodore E. H. Lee, Medical Director General, Royal Canadian Navy; Brigadier S. G. U. Shier, Director General of Medical Services, Army; and Air Commodore A. A. G. Corbet, Director General of Medical Services, Royal Canadian Air Force.

The Annual Meeting of the Defence Medical Association was held in Ottawa on November 22 and 23. The Coordinator of Medical Services, Brigadier K. A. Hunter, reported upon the history, aims and activities of the Canadian Forces Medical Council, and in his capacity as permanent Chairman of the Inter-Service Medical Committee, reported upon the activities of that committee.

Surgeon Commodore E. H. Lee, Medical Director General (Navy); Brigadier S. G. U. Shier, Director General of Medical Services (Army); and Air Commodore A. A. G. Corbet, Director General of Medical Services (Air) also reported to the Association upon the activities of their respective medical services.

Surgeon Lieutenant Commander (P) H. D. Oliver, RCN, who has been undertaking postgraduate training Naval Air Station at Dartmouth, Nova Scotia, has recently become a Diplomate of the American Board of Aviation Medicine.

Surgeon Lieutenant Commander D. V. Willoughby, RCN, who has been undergoing postgraduate training in surgery in Toronto, has recently obtained his certification in General Surgery.

Surgeon Commander M. C. Wellman, RCN, Principal Medical Officer, HMCS *Cornwallis*, was promoted to Acting Surgeon Captain on September 4, 1956.

Major W. Fowler attended the 86th Annual Meeting of the American Public Health Association at Atlantic City, November 12-16, 1956. The current status of the use of poliomyelitis vaccine, epidemiology of coronary sclerosis, automobile accident prevention, and the use of adenovirus vaccines were among the subjects discussed.

Group Captain B. R. Brown, C.D., and Group Captain G. D. Caldbick, C.D., have been made Fellows of the American College of Preventive Medicine in the specialty of aviation medicine.



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## BOOK REVIEWS

**LIONS IN THE WAY.** Anne Wilkinson. 247 pp. Illust. The Macmillan Company of Canada, Limited, Toronto, 1956. \$5.00.

The many Osler enthusiasts in the medical profession will find it profitable and entertaining to read this delightful history of the famous family by a great-niece of Sir William. Anne Wilkinson fills in many gaps in the Osler story, commenting shrewdly on the family letters and diary entries to which she has had access. In the Herries Saga, the dominating character is Judith Paris; in the present story the heroine is also a long-lived, courageous, indomitable woman. Ellen Osler, the mother of Sir William, lived to celebrate her 100th birthday, in 1906, and was certainly the queen of the Osler matriarchy. She came to Canada as the wife of an Anglican clergyman, Featherstone Osler, first a Cornish naval man and later one of the indefatigable men who civilized Upper Canada, at a time when Tecumseh, 40 miles north of Toronto, was frontier country and in the mission field. The young couple arrived at what is now Bond Head on the day Victoria became Queen, endured incredible hardships and produced a large family of whom some gained fame—Featherstone and Britton in the law, William in medicine, and Edmund in finance. But every family has its black sheep, and the Oslers were no exception; Edward became a chronic failure and Frank a shiftless remittance man.

The story continues through a more gentle phase of family life when Featherstone Osler was rector of Dundas, and the author skilfully traces the adolescence and adult life of the young Oslers, with considerable emphasis on the highlights of William's career. She ends her tale with the death of Sir William in 1919, and then produces a scintillating epilogue, full of charm and humour. The epilogue describes her life as a child from 1919 to 1924, at Craigleigh, the Toronto home of Sir Edmund Osler, her grandfather. The sketches of the family servants and the many visitors are beautifully done. Among the latter were Mrs. Pankhurst, then busy preventing venereal disease, and Harvey Cushing, an unpopular figure in the children's world. It is recalled that Winston Churchill had stayed there and "did not shine as a house guest. The pillows did not suit; neither did this and neither did that. When told the family never dressed for Sunday supper Winston replied 'I do' and did".

Anne Wilkinson already has a reputation as a poet. With this biography she establishes a claim as a writer of fine prose as well. The book is essential for the lover of Canadiana, the Osler enthusiast, or just the person who likes to read well-written family history. And what a family to write about!

**THE HUMAN BODY. Its Anatomy and Physiology.** C. H. Best, Professor and Head of Department of Physiology, University of Toronto, and N. B. Taylor, Professor of History of Medicine and Medical Literature, University of Western Ontario, London. 723 pp. Illust. 3rd ed. Henry Holt and Company, New York, 1956. \$6.75.

The claim by the authors that this well-known introduction to anatomy and physiology has been altered and extended is borne out by study of the text. Whereas formerly the emphasis was on physiology, anatomical description now takes up a goodly part of the book. The anatomical descriptions of bones, muscles, blood vessels, and so on are well illustrated by drawings which have been specially made for the book. The authors justly complain that the description of elementary anatomy is hindered by the variety of nomenclature now available,

but have made a wise choice in their own terminology.

They have now added a glossary to the book, giving Latin, Greek or other derivations of medical terms, together with a definition. A new appendix contains such useful information as weights and measures with metric and other equivalents, comparative temperature scales, classifications of proteins and a list of their constituent amino acids, dietary tables and standard tables of weight in relation to height and age. A bibliography is given at the end of the book for those seeking more detailed information.

The text continues to prove a valuable and eminently readable guide to the construction and functions of the human body.

**DERMATOLOGY.** D. M. Pillsbury, Director, Department of Dermatology, W. B. Shelley, Associate Professor of Dermatology, and A. M. Kligman, Associate Professor of Dermatology, University of Pennsylvania School of Medicine, Philadelphia. 1331 pp. Illust. W. B. Saunders Company, Philadelphia and London, 1956. \$20.00.

This is a new textbook encompassing the entire field of dermatology, written, not merely compiled, by recognized authorities. It is inevitable in assessing the merits of any new work of this kind that we compare it with its appropriate predecessors.

This is a first edition, and, as such, the continuity of its prose and thought enhance its readability, in contrast to the older texts in which this quality has been increasingly destroyed by the deletions and additions of succeeding revisions. A radical departure from standard practice is the virtual absence of pertinent references, which will undoubtedly constitute a serious adverse criticism for some readers but by no means for all. The decision in this regard was not made without due consideration and reasons for it are outlined in the preface.

The first five sections of the book, constituting more than a quarter of the whole, are devoted to basic pertinent subjects with discussions of anatomy, physiology, bacteriology, mycology, allergy, and principles of diagnosis and treatment. At the conclusion of many of the chapters in these sections are capsule summaries which should appeal to the "digest" type of reader. The intensely fascinating recent research elucidating the physiological processes of pigmentation and keratinization is clearly presented and the notoriously complex, confusing subject of allergy is presented in an organized, lucid fashion. To this reviewer, the de-emphasis of the role of allergy in the etiology of atopic eczema is particularly welcome.

In the ensuing chapters dealing with specific disease entities, where etiology is unknown, little space is devoted to diverse conflicting opinions and theories. Pictures, although not in colour, are carefully chosen and presented to depict outstanding differential features, and the quality of photographic reproduction is excellent. The cartoon form of diagram is used to good advantage in many cases for depicting mechanisms of disease production. A sincere effort has been made to modernize and simplify nomenclature by eliminating pompous complex terminology. The presentation of treatment is particularly commendable. For those diseases in which one or two methods of treatment are outstanding, this is so stated, and for diseases in which several methods of management must sometimes be tried, the order of preference is given. Frank statements are made where treatment is unavailing.

Although this work will not replace the older standard textbooks for reference purposes, it does satisfy a real need and undoubtedly will take its place with them as a welcome complement. For the student, the size and cost may be prohibitive. For the specializing dermatologist, there is much of value; for those others interested in or dealing with dermatological problems, there is a great deal of value.

**LOVE AND SALT WATER.** Ethel Wilson. 203 pp. The Macmillan Company of Canada, Limited, Toronto, 1956. \$2.50.

Those who have not yet made the acquaintance of Ethel Wilson's novels should be told that they are neglecting a Canadian writer of real distinction. Her latest book, *Love and Salt Water*, is as usual set mostly in the British Columbia she loves so well, but there is nothing parochial about her outlook, and it is clear that she has an unusually fine concept of and love for the whole Canadian scene.

The present book tells the love story of Ellen Cuppy, who as a teenager accompanies her widowed father on a voyage, disappears from our view for a few years during the war, comes back to Vancouver to reject a bad-tempered suitor, goes to work in Saskatoon, and finally yields to the persistence of another suitor after a boating accident which nearly wrecks her whole life.

It is a lean, spare novel without any superfluous fat. Mrs. Wilson employs the opposite of the Balzac technique, and can sketch in the first 30 years of a character's life in two or three sentences. Her unique style is well illustrated by the sentence below: "She, Huw's mother, is probably one of those women who like everybody, and it is sufficient to have met someone once on a train to incur reciprocal visits and Christmas cards for ever." It is difficult to believe that this thought could have been expressed in fewer words.

The plot is slight, yet the book carries the reader on smoothly, though the middle portion, between the drama of the voyage with its beautifully described storm at sea and the high excitement of the boat accident, is somewhat tranquil. But Ethel Wilson has the gift of retaining interest in tranquillity. Her sensitive imagination and charm of style assure her continued place as an important Canadian writer.

**THE GREAT PHYSIODYNAMIC THERAPIES IN PSYCHIATRY.** An Historical Reappraisal. Edited by A. M. Sackler, Editor, *Journal of Clinical and Experimental Psychopathology*, and others. 190 pp. Paul B. Hoeber, Inc., Medical Book Department of Harper & Brothers, New York, 1956. \$5.75.

This is a very interesting and well-written book. A certain amount of continuity is lost because the various chapters are written by different people. However, the authors are all experts on their subjects and pioneers in the more effective physical treatments of certain psychiatric disorders. The last chapter is of particular interest, as an attempt is made to project into the future of further developments in this particular phase of psychiatric treatment.

It is fascinating to learn at first hand about the development of treatments such as insulin coma, E.C.T.

and prefrontal leukotomy, which have now assumed such an important and accepted place in the treatment of mental illness. In each instance the original hypotheses have been discarded and to the present day there remains considerable conjecture about the *modus operandi*. Nevertheless, the effectiveness and usefulness of these treatments in appropriate cases has become well established.

This book is especially timely in view of the present trend to focus once again on the physical aspects of psychiatric disorders. There is still, unfortunately, a tendency to split the physiodynamic and psychodynamic approaches to this problem. The physiodynamic approach is presented very well in this book and should prove stimulating to any student of psychiatry.

**CLINICAL HEMATOLOGY.** M. M. Wintrobe, Professor and Head, Department of Medicine, University of Utah, College of Medicine, Salt Lake City. 1184 pp. Illust., 4th ed. Lea & Febiger, Philadelphia; The Macmillan Company of Canada Limited, Toronto, 1956. \$15.00.

This remarkably up-to-date book on hæmatology is now in its fourth edition. The greater proportion of the text of the third edition has been extensively modified and revised. In addition, two new chapters have been added, one on blood groups and transfusion, the other on abnormal hæmoglobin syndromes and inherited disorders of the erythron.

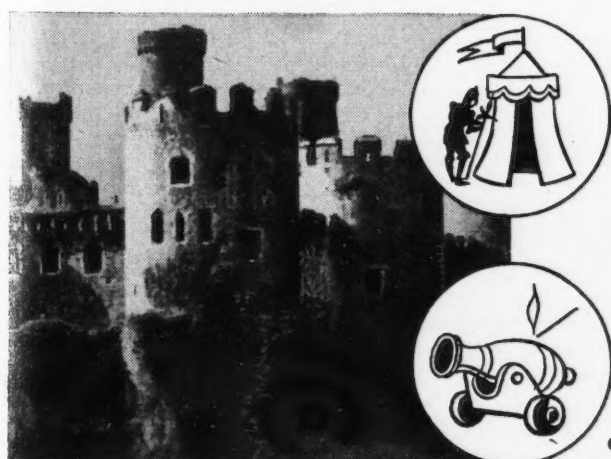
The author has enlarged upon, rewritten or almost completely revised the chapters that deal with the coagulation of the blood and hæmorrhagic disorders, and the production and destruction of erythrocytes under normal circumstances or in diseases characterized by hæmolytic anæmia.

The cytochemistry of the bone marrow has been dealt with in some detail. The function of ribonucleic acid (RNA) and desoxyribonucleic acid (DRNA) in the proliferation and maturation of cells, and the role of vitamin B<sub>12</sub> and folic acid in the production of nucleic acid, are clearly discussed. Newer techniques for the measurement of blood production and destruction such as the use of the scintillation counter for the determination of the incorporation of Fe<sup>59</sup> into red cells, or the estimation of erythrocyte life span by tagging the red cells, have been included.

The many charts on the therapeutic management of leukæmia with folic acid antagonists, alkylating agents, Myleran, purine analogues, urethane, steroids, or irradiation are most useful. They clearly point out the advantages and dangers of these various kinds of therapy.

The bibliography is most extensive. The author states that 1600 new references have been added.

This book is highly recommended as a reference work for student, practitioner and internist alike.



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**LEITFADEN DER NEUROLOGIE** (A Guide to Neurology). F. Laubenthal. 315 pp. Illust. 6th ed. Georg Thieme Company, Stuttgart; Intercontinental Medical Book Corporation, New York, 1956. \$7.10.

This is a book for the beginner in neurology. It consists of two parts: the first contains a description of the methods of investigation used in neurology, and the second gives a brief description of neurological syndromes and diseases. In the latter, emphasis is on clinical description, with a minimum space devoted to therapy. The book is well produced, clearly written and profusely illustrated.

**LECTURES ON THE SCIENTIFIC BASIS OF MEDICINE**. Vol. 4, 1954-55. General editor, F. R. Fraser, Director, British Postgraduate Medical Federation. 397 pp. Illust. University of London, The Athlone Press, 1956. 37s.6d.

The British Postgraduate Medical Federation continues its good work of providing courses of lectures on the basic sciences for research workers or for those approaching specialization in various fields of medicine. The present volume contains 21 lectures, beginning with a discussion of the meaning and scope of biophysics by Professor A. V. Hill. He describes biophysics as the study of biological function, organization and structure by physical and physico-chemical ideas and methods, putting ideas first, since physical techniques and instruments may be used in any field of research. He shows that the physicist who develops a biological approach and wanders into the field of biophysics is no longer regarded as an oddity by his fellow physicists. Dr. C. H. Andrewes gives a conspectus of virus research today

in a lecture entitled "The New Look in Virus Research". Other lectures illustrate various aspects of biological chemistry, physics and pharmacology. Many are in close relation to clinical science, for example, the lecture on the chemistry of the porphyrias and the contribution on protein malnutrition. The surgeon will be interested in contributions on shock from burns, the electrolyte and metabolic response to trauma, cooling of the whole organism, and the comparative anatomy of the larynx. Dr. Gaddum has a characteristically entertaining contribution on the effects of alcohol. The volume ends with a valuable contribution by Pearse on histochemistry and its application to the basic sciences. Physicians puzzled by some of the newer developments in the basic sciences will find this volume a mine of information.

**THE ORGANIZATION OF THE CEREBRAL CORTEX**. D. A. Sholl, Reader in Anatomy, London University. 125 pp. Illust. Methuen & Co. Ltd., London; John Wiley & Sons, Inc., New York; The Ryerson Press, Toronto, 1956. \$3.75.

This author has studied the human cerebral cortex histologically from the point of view of the quantity of its contained nerve cells. In silver-stained sections he has studied in detail the variabilities in the types of processes of these cells. In the "classical" 2nd, 4th, 5th and 6th cortical layers the majority of the cells have long axons arising from the base of the cell and long apical dendrites extending to the "molecular" or 1st cortical layer. The 3rd or "stellate" cortical layer, on the other hand, consists mainly of cells with multiple small dendrites and a short axon, which ends near its parent cell.

From these anatomical studies he is able to discuss the organization of the cortex from the mathematical and statistical angles. This new approach to the study of cortical function is in line with recent developments in mathematical research.

The author acknowledges his great debt to Professor K. S. Lashley, who has maintained for many years that the "quantity" of cortical tissue removed from an experimental animal is of more significance than the "quality" of any particular area.

**MULTIPLE NEUROFIBROMATOSIS**. A Clinical, Pathological and Genetic Study. F. W. Crowe, Department of Dermatology, School of Medicine and Heredity Clinic, Institute of Human Biology, W. J. Schull and J. V. Neel, Heredity Clinic, University of Michigan, Ann Arbor. 181 pp. Illust. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1956. \$5.50.

This is an excellent book of 181 pages, attractively printed and well arranged, with good type and paper. The study was conducted at the University of Michigan, in the School of Medicine and Heredity Clinic. In contrast to the many isolated case reports appearing in medical literature, this study gives a representative picture of 223 patients for each of whom triple investigations were carried out, namely, clinical, pathological and genetic.

The conclusion is reached that the diagnosis of neurofibromatosis can be made with certainty, and on the basis of these reliable data the genetic calculations are carried out. The frequency of the disease is calculated as between 1 in 2500 and 1 in 3300 births.

The condition is shown to be inherited through a dominant gene with a high level of penetrance. The reduction in fertility of the affected persons is discussed and calculations are made as to the possible mutation rate of the gene for neurofibromatosis.

This is a very modern medical report, suitable for inclusion in courses in medical genetics and for the discussion of problems which the younger generation of physicians are facing.

(Continued on advertising page 40)

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## BOOK REVIEWS

(Continued from page 172)

**HYPOTHALAMUS UND THALAMUS.**  
Experimental Dokumente (Documen-  
tary Pictures). W. R. Hess, Zurich.  
70 pp. Illust. Georg Thieme Com-  
pany, Stuttgart; Intercontinental  
Medical Book Corporation, New  
York, 1956. \$8.60.

This excellently produced book is, as its author states, simply a condensed atlas of his own findings in stimulation experiments with cats. It covers the period 1924-1951. "[The 400 experiments] demonstrate the relationships between the responses elicited and the corresponding points of stimulation." The responses studied are autonomic and motor. The book is the third of a series dealing with Professor Hess's work in the Physiological Institute, Zurich. The text is in both German and English. The bibliography (89 references) is of work emanating from the Physiological Institute.

**DIE BEHANDLUNG DES BLUT-  
HOCHDRUCKES** (Treatment of  
Hypertension). L. Hantschmann, Rem-  
scheid, W. Germany. 92 pp. Illust.  
Georg Thieme Company, Stuttgart;  
Intercontinental Medical Book Corpo-  
ration, New York, 1956. \$2.85.

In this practical monograph Hantschmann notes the rising incidence of hypertension in Germany, associated with overeating and increase in nervous tension. This book is a description of the present (unsatisfactory) position in therapy of hypertension, with only as much about diagnosis and pathogenesis as is necessary for understanding of therapeutic principles.

The chapters on therapy first dispose of the unusual types of hypertension, such as hypertension associated with pheochromocytoma, and then give a useful, detailed account of the treatment of the essential type, including diet, drugs and surgery. There is an up-to-date bibliography.

**TERRAMYCIN (Oxytetracycline).** Anti-  
biotics Monographs No. 6. M. M.  
Musselman, Professor of Surgery,  
University of Nebraska College of  
Medicine, Omaha. 144 pp. Medical  
Encyclopedia, Inc., New York; Inter-  
science Publishers, Inc., New York,  
1956. \$4.00.

This is one of a series of monographs on the individual antibiotics in which the use of this particular one is discussed in considerable detail, with a great deal about its basic pharmacology and chemistry. One feels that some of the clinical evaluations are not sufficiently critical, and in general the discussion of various specific disease states consists mainly of a recital of the various reports in the literature. The author minimizes the toxic reactions and dangers of the drug rather more than one would like to see. In general the book does not appear to be as authoritative and useful from the point of view of coming to definite therapeutic conclusions as it could be, but it does provide a useful source for references on the subject.

**POLYMYXIN, NEOMYCIN AND  
BACITRACIN.** E. Jawetz, Professor  
of Microbiology, University of Cali-  
fornia. 90 pp. Medical Encyclopedia  
Inc., New York; Interscience Pub-  
lishers, Inc., New York, 1956. \$4.00.

These three antibiotics are included together in one monograph because they are all polypeptides, because when used systemically they have a degree of toxicity, which renders their use in this field rather infrequent, and because they are commonly used together in various combinations in ointments or surface applications to good effect. They are bactericidal and have a very low sensitizing potential. The author emphasizes that all three can be used with great advantage in serious infections with organisms resistant to other antibiotics in spite of their toxicity, which is by no means prohibitive if the dosage is carefully controlled, the patient's fluid intake and urinary output watched carefully and the presence of pre-existing renal disease ruled out. The main use of polymyxin is in infections due to *B. pyocyaneus* (*Pseudomonas*) whereas bacitracin finds its greatest value in staphylococcal infections. Neomycin has much the same spectrum as streptomycin and so is useful in occasional staphylococcal infections and infections caused by Gram-negative bacilli resistant to the more ordinary antibiotics. Useful details of the pharmacology and clinical application of these substances are included in the volume and the clinical evaluations of the results in various types of disease seem to be very fair and authoritative.

**THALLIUM POISONING.** J. J. Prick,  
Professor of Neurology, Nijmegen  
University, W. G. S. Smitt, Professor  
of Neurology, Utrecht University, and  
L. Muller, Industrial Physician,  
Enschede, The Netherlands. 155  
pp. Illust. Elsevier Publishing Com-  
pany; Burns & MacEachern, Toronto,  
1955. \$3.95.

Here is a medical monograph which begins like a detective story with the account of a series of criminal poisonings due to thallium in Holland during the war. Details of the clinical course of these patients are presented, after which a survey of the experimental and pathological evidence regarding the nature of thallium poisoning is presented from the literature and from the authors' own data.

The manifestations of thallium poisoning may be acute with fever, delirium, ascending paralysis, muscle pains and gastro-intestinal disturbances. On the other hand, they may be more chronic, in which case the patient's hair falls out and pigmentation of the skin occurs, with frequent ocular disturbances, peripheral neuritis and sometimes psychosis.

The authors point out the possible sources of thallium poisoning and the great danger that criminal poisoning with thallium sulfate, which is completely odourless, tasteless and delayed in its action, may escape detection.

Chemical methods of estimating thallium in the urine and body fluids are available and described in the monograph.

(Continued on page 42)

## Assignment:

# BROAD TARGET

PEN • VEE-S Tablets combine  
PEN • VEE (penicillin V), the new  
acid-stable penicillin, with the highly  
effective sulfonamides—sulfadiazine  
and sulfamerazine, for broad  
therapeutic coverage



### ★ INDICATIONS:

Hemolytic streptococci	diseases of the upper respiratory tract and urinary tract; erysipelas, impetigo, cellulitis
Pneumococci	pneumonia
Meningococci	meningitis
Staphylococci	often implicated in diseases of the meninges, lungs, bone, skin and urinary tract
Gonococci	diseases of the eye, urethra, joints
Ps. aeruginosa, Str. faecalis and E. coli	diseases of the urinary tract
Hemophilus influenzae	laryngotracheobronchitis, pneumonia
and	in certain types of bacillary enteritis caused by some Shigella and coliform organisms



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### TABLETS

Penicillin V and Sulfonamides

Supplied: Each tablet contains 90 mg. (150,000 I.U.) penicillin V, 0.25 Gm. sulfadiazine and 0.25 Gm. sulfamerazine; bottles of 12 and 100 scored tablets.

- active against many gram-positive and gram-negative bacteria
- has synergistic or additive action, particularly valuable in mixed infections
- reduces possibility of emergence of drug-resistant organisms

**P** available on prescription only

\*Trade Mark





## BOOK REVIEWS

(Continued from page 40)

**DIE LUNGENTUBERKULOSE.** Diagnose und Therapie. (Pulmonary Tuberculosis. Diagnosis and Therapy.) P.-G. Schmidt, Waldbreitbach, W. Germany. 384 pp. Illust. 3rd ed. Georg Thieme Company, Stuttgart; Intercontinental Medical Book Corporation, New York, 1956. \$13.80.

Although the subtitle of this volume is Diagnosis and Therapy, chapters on the history of tuberculosis, pathogenesis, pathological anatomy, allergy and immunity, and on some forms of extrapulmonary tuberculosis, are included. As

the author points out in the preface, he considers the time has come for a review of treatment results with tuberculostatic drugs and for an outline of proper indications for surgical therapy. In the text, however, much space is devoted to methods of treatment which, at least on this continent, are not used at all or are losing significance. Among the newer drugs thiosemicarbazones and PAS infusions are discussed at length, while the generally accepted long-term combined drug therapy is barely mentioned. Among the surgical methods of treatment, considerably more space is devoted to collapse therapy than to resections.

In summary, this book cannot be considered as an up-to-date text on tuberculosis as measured by North American standards. Print and illustrations are excellent.

**WILLIAMS OBSTETRICS.** N. J. Eastman, Professor of Obstetrics, Johns Hopkins University, and Obstetrician-in-Chief to the Johns Hopkins Hospital, Baltimore, Md. 1212 pp. Illust. 11th ed. Appleton-Century-Crofts Inc., New York, 1956.

Dr. Nicholas J. Eastman has for many years been an authoritative speaker at medical meetings. The author's comments on medical papers have been thoroughly sound in every detail. The entire contents of this new textbook of obstetrics are in no wise different in quality from the above comments, with which we are all familiar.

The new edition is up-to-date in every detail, pleasant to read and sound in practice. This obstetrical textbook is an excellent guide for medical students, practitioners and specialists. Dr. Eastman's book cannot be too highly recommended.

**HANDBUCH DER ALLGEMEINEN PATHOLOGIE** (Handbook of General Pathology). Vol. VI, Part III. Tumours. Edited by F. Buchner, Freiburg, W. Germany. 493 pp. Illust. Springer Company, Berlin, W. Germany, 1956. 120 marks.

This is the most recent number in the 12-volume *Handbook of General Pathology*, most of which is still in preparation. Anyone familiar with the monumental works issued by the publishing house of Springer will be glad to know that the standard of production is as high as ever in the present series. In the introduction to the present volume, Albertini of Zurich discusses the classification of tumours, with special reference to Willis's views, pointing out that the disorderly behaviour of neoplasms renders any logical classification difficult. Hamperl of Bonn then considers the morphology of tumours beginning with the characteristics of the tumour cell, passing on to tumour tissue, and finally dealing with the various modes of tumour growth.

A monograph on the biochemistry of tumours by Butenandt and Dannenberg of Munich follows, with an equally long section (almost 100 pages) by Domagk on experimental tumour studies. Walther Fischer of Jena discusses the more important endogenous and less important exogenous factors in the etiology of tumours, appending to his discussion an addendum reviewing the work prepared at the Congress of the International Association for Geographical Pathology, 1954, Washington.

All these chapters contain a remarkably comprehensive review of the literature. Domagk for instance lists something like 1,500 papers in his bibliography, from all parts of the world. The general impression from this volume is one of immense industry coupled with careful evaluation of contributions to the literature of tumours.

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or a **PRURITIC** symptom

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ointment  
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## Extract from a report on some one hundred cases:

"We found the Metanium products to be safe therapeutic agents for use by the profession at large. The use of both ointment and powder was undertaken in a variety of inflammatory dermatological conditions and was attended by uniformly satisfactory results."

Ereaux, L. P.: "Clinical observations on the use of Titanium salts in the treatment of dermatitis." C.M.A.J. Vol. 73, No. 7, July 1955.

## Summary of a study on 90 patients:

"Ninety patients were treated with an ointment and powder containing the salts of Titanium (Metanium). Our experiments were conducted mainly on eczematous and eczematiform skin diseases. These experiments have shown that the salts of titanium have now placed themselves advantageously at the side of medications composed of hydrocortisone. In certain cases they have proved themselves superior. They are absolutely innocuous and their price is moderate."

Poirier, P., and Baillargeon, Y.: "Clinical observations on the use of Titanium salts (Metanium) in the treatment of certain skin diseases." L'Union Medicale, Vol. 85, No. 4, April 1956.

**The Leeming Miles Co. Ltd., Montreal 28**

## MEDICAL NEWS in brief

(Continued from page 140)

### FLUORIDATION IN THE SOVIET UNION

It is often forgotten that the greatest experience with fluoride and dental caries has been obtained in the Soviet Union, where local application of fluoride to teeth began in 1935 and the first results were published in 1937. Work has been done on a large scale since 1948. Water supplies are not fluoridated, but the technique is to apply for a few moments to the teeth a glycerinated paste containing 75% of sodium fluoride. The mouth is washed out and rinsed out, and the operation is performed twice a year for children six to 12 years old. Each school paediatrician treats 2000 - 3000 children. All those who have used the method confirm that there is a significant reduction of dental caries in controlled studies. Where the molars of one side have been treated, the caries incidence has been 1.4% as against 20.2% in controls. A decrease in caries is also claimed when the treatment is applied to pregnant women.

### DRUG INFORMATION SOURCES

In view of the great speed with which new drugs appear on the market and the immense volume of material now available, all those concerned with drug therapy will welcome the announcement by the Pharmaceutical Section of the Special Libraries Association that its bibliography, "Drug Information Sources", will be published as a regular feature of the *American Journal of Pharmacy* starting in January 1957. "Drug Information Sources" will be an annotated list of drug encyclopædias, codices, dispensatories, price lists and related sources supplying information about drugs. It will appear in monthly instalments, each instalment covering information sources of a few countries. The list will be revised as needed to keep it up to date. Requests for information about the bibliography should be addressed to Miss Anne McCann, Chairman of Drug Information Sources Committee, Library, Squibb Institute for Medical Research, New Brunswick, N.J.

### HEALTH HABITS AND HEART DISEASE

Dr. Luongo of Los Angeles (*J. A. M. A.*, 162: 1021, 1956) emphasizes once more the role of good nutritional habits and an exercise pattern in the prophylaxis of coronary disease in men. He has begun this study of 100 proven cases of manifested coronary disease in comparison with 200 control cases in the same age group. Only one of these patients was a

woman. He notes that more than two-thirds of the patients with coronary disease were overweight or obese on the average for 10 to 15 years before their attack, while only one-third of the controls fell into this category. Exercise also appeared to be correlated with coronary disease, for 70% of those who sustained coronary incidents had no regular exercise pattern either at work or away from the job, whereas only 30% of controls

(Continued on page 48)

in the PROPHYLAXIS of  
ANGINA PECTORIS ATTACKS<sup>1</sup>

in the RELIEF of  
TENSION HEADACHES<sup>2</sup>

## METAMINE®

tablets of 2 mg.

triethanolamine trinitrate biphosphate

1 tablet every 4 hours

Exerts prolonged action without deleterious effect.

Produces no significant change in the mean blood pressure level.

### Conclusions from a recent study on 40 patients:

1. "From our observations it appears that Metamine in the usual dosages is a powerful agent in the treatment of angina pectoris. One tablet (2 mg.) of Metamine, three times a day, produced satisfactory results in controlling anginal pains in the great majority of our patients. There was no evidence of toxicity to Metamine in this group of patients nor increased tolerance to this drug. Hypotensive manifestations like headaches or throbbing in the temples were not observed in this study."

Rivas, F. D., and Rivera, R. S. D.: "The use of Metamine in angina pectoris." *BOLETIN de la Asociacion Medica de Puerto Rico*, Vol. 48, No. 6, June 1956.

### Conclusions from a recent study on 80 patients:

2. "Triethanolamine trinitrate biphosphate in oral doses of 2 to 5 mg. was analogously effective in 80% of 80 patients whose vasculographic records gave evidence of temporal artery constriction and temporal muscle contraction headache."

Tunis, M. M.: "Cranial artery vasculography and (extra) cranial headache." *C.M.A.J.*, Vol. 74, No. 3, February 1956.

The Leeming Miles Co. Ltd., Montreal 28



## MEDICAL NEWS in brief

(Continued from page 47)

had no regular exercise pattern. No correlation was found with the use of tobacco or alcohol, though Dr. Luongo is quick to point out that this does not mean either that tobacco is without harmful effects on already diseased coronary arteries or that alcohol is beneficial in improving coronary blood flow. There is no absolute correlation between occupation and coronary

disease, except that employees in sedentary occupations tend to neglect their nutrition and exercise.

### PROGNOSIS IN SHOULDER DISLOCATIONS

In the *Journal of Bone and Joint Surgery* (38A: 957, 1956) Rowe analyzes 500 cases of dislocation of the shoulder with particular reference to prognosis. The series included patients treated over a

20-year period, with a mean follow-up of nearly five years. The dislocation recurred in 38% of patients. Contrary to the general opinion, this series showed an equal division of primary dislocations before and after the age of 45. However, recurrence was most likely in younger patients, particularly in the second decade of life. The age of the patient at the time of the primary dislocation was the most significant prognostic factor. The greater the initial injury, the less likely was the dislocation to recur. In 24% of cases the shoulder girdle was fractured, with an incidence of fracture of the greater tuberosity of 15%. In 38% of primary dislocations and 57% of recurrent ones, there was a defect of the humerus, associated with an increased likelihood of recurrence. Incidence of recurrence was little affected by type and length of immobilization of shoulder after dislocation. In 70% of recurrences, the second dislocation occurred within two years. After operation for repair of recurrent shoulder dislocation, 52% still recurred within two years.

A follow-up of 75 cases in which the Bankart operation was carried out for recurrent dislocation indicated that this procedure is very dependable.

### NEPHROGENIC DIABETES INSIPIDUS

At the meeting of the Royal College of Physicians and Surgeons of Canada in Toronto recently, a paper was read on the unusual condition known as "nephrogenic diabetes insipidus", which is a sex-linked condition characterized by polyuria dating from infancy and resistant to the pituitary hormone, vasopressin, renal function being otherwise normal. Patients not kept fully hydrated develop mental defect and may die young. It is of practical importance to detect women who are heterozygous for those sex-linked genes which cause severe disability in males. It is of particular importance to detect them in this type of diabetes insipidus because untreated patients may die early. At the Hospital for Sick Children, London, England (*Lancet*, 2: 1069, 1956) Carter and Simpkins have evolved a test which they applied in four families to mothers, maternal grandmothers and other female relations who

*quicker relief  
and shortened disability  
in Herpes Zoster and Neuritis*

## Protamide®

### ... Five Year Clinical Evaluation

With only one to four injections of Protamide® prompt and complete recovery was obtained in 84% of all herpes zoster patients and in 96% of all neuritis patients treated during a five-year period by Drs. Henry W., Henry G., and David R. Lehrer (Northwest Med. 75:1249, 1955).

The investigators report on a total of 109 cases of herpes zoster and 313 cases of neuritis, all of whom were seen in private practice. All but one patient in each category responded with complete recovery.

This significant response is attributed to the fact that Protamide therapy was started promptly at the patient's first visit.

The shortening of the period of disability by this method of management is described as "a very gratifying experience for both the physician and the patient."



Protamide® is a sterile colloidal solution prepared from animal gastric mucosa... free from protein reaction... virtually painless on administration... used intramuscularly only. Available from supply houses and pharmacies in boxes of ten 1.3 cc. ampuls.

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might be heterozygous for the gene responsible for nephrogenic diabetes insipidus. The women were asked to drink no water after 7 p.m., to pass urine before going to bed at 11 p.m., and to collect the first morning specimen of urine. The authors found that in heterozygous women the mean specific gravity in three morning specimens of urine did not exceed 1.018. Diagnosis on the basis of this urine-concentration test agreed well with genetic analysis of the four pedigrees.

### TUBERCLE

Our attention is drawn to the fact that *Tubercle*, the journal of the British Tuberculosis Association and a well-established publication in this field, has changed its format since the beginning of 1956 and is now appearing every two months in an enlarged size. In addition to this enlargement and improvement in make-up, the journal now covers the entire field of respiratory disease, including laboratory and epidemiological aspects. Dr. J. R. Bignall of the Institute of Diseases of the Chest, Brompton Hospital, London, has recently been appointed editor. The December number of the journal contains original articles on tuberculin insensitivity in pulmonary tuberculosis, the pathological and bacteriological examination of resected lung specimens, clinical trials of chemotherapy in African patients, the vole bacillus and mass radiography surveys.

### EXPERT COMMITTEE ON RABIES

The third WHO Expert Committee on Rabies met at the Pasteur Institute, Paris, from November 26 to December 1. Dr. Pierre Lépine of Paris was elected chairman. Dr. Koprowski of Pearl River, U.S.A., was reporter. The most important thing discussed was the treatment of rabies. It has now been shown that serum plus vaccine is strikingly effective in preventing rabies, although it is necessary to give a complete course of vaccine along with the serum therapy. Persons must also be tested for serum sensitivity before the latter is used. Studies have shown the value of immediate cleansing of suspected

injuries with soap and water, followed by cauterizing with nitric acid where possible, and injection of serum around the site of the bite.

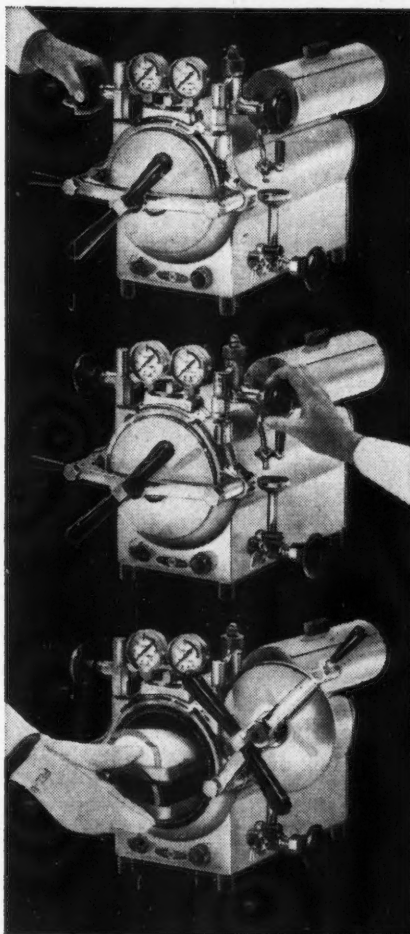
Persons exposed to repeated bites, such as laboratory workers and postmen, are given basic protection by very small doses of chicken embryo vaccine or a few doses of ordinary nervous tissue vaccine, followed by a single booster dose if they are bitten. Improved vaccines for domestic animals were also discussed.

### HYPNOSIS IN THE CASUALTY DEPARTMENT

A London physician describes the use of hypnosis in unselected cases seen in the casualty department of a general hospital (*Brit. M. J.*, 2: 1340, 1956). He suggests that hypnosis or suggestion be used in the casualty department in treatment of minor injuries, as an adjunct to the anaesthetic facilities, since it reduces the number of

(Continued on page 50)

## WHY BOIL?



when you can sterilize  
**FASTER and SAFER**  
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## PELTON AUTOCLAVE

So Easily Operated

### TRANSFER

After loading, simply transfer steam from reserve to sterilizing chamber. In only a few seconds, temperature is attained.

### DISCHARGE

When sterilization is completed, discharge steam to condenser after closing transfer valve and crack open the door.

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In a minute or two entire contents are removed completely sterile and dry. The autoclave is ready for second load.

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Model FL-2,  
6" x 12" sterilizing chamber

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## MEDICAL NEWS in brief

(Continued from page 49)

anæsthetics that need to be given, and therefore the time spent in waiting for digestion of a recent meal. It also economizes the anæsthetist's time. The technique can be effective with untrained subjects.

Conditions treated under hypnosis included reduction of fractures, replacement of dislocations, dental extractions, suturing of incisions and nail avulsions.

BENZTROPINE IN  
PARKINSONISM

Doshay of New York (*J. A. M. A.*, 162: 1031, 1956) describes a five-year study of a relatively new synthetic drug, bengtropine (Cogentin) methanesulfonate, in 302 cases of Parkinsonism. The drug has anticholinergic, antihistaminic and sedative actions. It has a prolonged cumulative and very useful peripheral curariform effect. The best results in controlling rigidity, contracture, tremor and insomnia

were obtained with a dosage range of 1-4 mg. a day for older patients, and 2-8 mg. for younger ones. The drug has been in continued use in some cases for more than five years and appears to be safe.

CONTROLLED TRIAL  
OF MEPROBAMATE

From St. Thomas's Hospital, London (*Brit. M.J.*, 2: 1206, 1956), comes the report of a clinically controlled trial of meprobamate (Equanil, Miltown) in 151 psychiatric outpatients. This tranquillizer produced some relief of symptoms in 58% of patients with chronic anxiety and tension states. Its effect was not so good when anxiety or agitation was severe. In a double blind trial carried out on 26 patients with anxiety and tension, the results of meprobamate were statistically significant in comparison with those of the placebo. In another double blind trial meprobamate was compared with sodium amylobarbitone (Amytal) in 51 patients with anxiety and tension; no marked differences were found in effectiveness, but meprobamate seemed more useful where the patient was irritable. No serious side-effects were observed, but transient skin rashes appeared in five patients.

AMERICAN MEDICAL  
ASSOCIATION AWARD  
FOR TV SERIES

At Seattle, on November 28, the American Medical Association cited Ciba Pharmaceutical Products, Inc., Summit, N.J., for service to the medical profession through its presentation of the national television series, *Medical Horizons*.

A.M.A. president, Dr. Dwight H. Murray, presented the citation before the Association's House of Delegates assembled for its annual meeting.

*Medical Horizons* presents "live" documentary reports on the latest developments in medical science each week directly from hospitals, clinics, and laboratories. The series, now in its second year, is presented with the co-operation of the American Medical Association, and is seen every Sunday afternoon at 4.30 p.m. (EST) over the ABC television network.

(Continued on page 52)

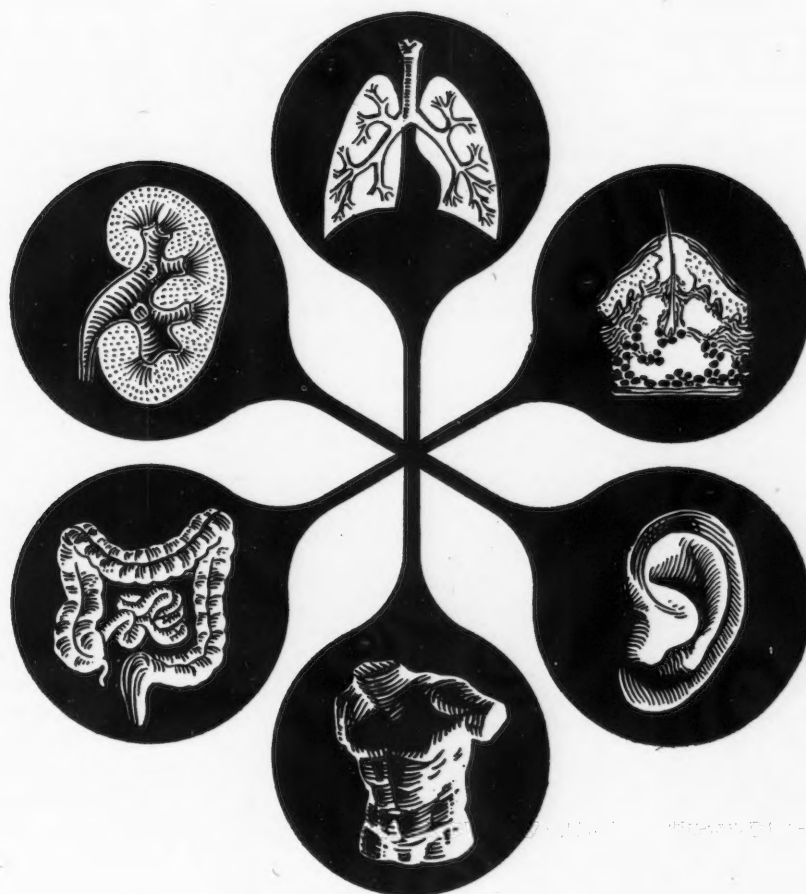
**FURACIN**\*

BRAND OF NITROFURAZONE

Proven Wide-range Bactericide for Prevention  
and Treatment of Topical Infections.SURFACE INFECTIONS  
Dressing . Powder . SolutionEYE  
Ointment . LiquidEAR  
Anhydrous Solution . PowderNOSE  
Liquid with vasoconstrictorURETHRA  
Suppositories . SolutionVAGINA  
Suppositories . Solution . Powder

- wide range of antibacterial activity
- negligible development of bacterial resistance
- effective in blood, pus and serum
- used topically only — does not interfere with future systemic medication
- facilitates healing by control of mixed infections
- minimizes malodour and drainage
- negligible tissue toxicity

AUSTIN LABORATORIES LIMITED  
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*when the clinical problem is a "common" infection*

OF TISSUE, TRACT OR SYSTEM

*Albamylin\**

**BECAUSE:** Blood concentrations with orally-effective Albamylin are 10 to 50 times higher than with other antibiotics, and significant serum concentrations persist 24 hours or longer; a broad therapeutic range is provided by bactericidal activity against Gram-positive and a certain few important Gram-negative pathogens (including susceptible strains of staphylococci and *Proteus* resistant to other antibiotics); clinical response is prompt in the majority of common infections; gastro-

intestinal tolerance is excellent; cross-resistance with other commonly used antibiotics is unknown.

**Adults:** 500 mg. every 12 hours. **Children:** 15 mg./Kg. of body weight per day, in divided doses every 6 or 12 hours. **Supplied:** Albamylin Capsules, 250 mg., bottles of 16. Albamylin Syrup (125 mg. per 5 cc. teaspoonful), bottles of 2 fluidounces.

\*TRADEMARK FOR UPJOHN'S BRAND OF NOVIOBICIN

**Upjohn**

Fine pharmaceuticals since 1886  
THE UPJOHN CO. OF CANADA  
865 York Mills Rd., Box 202  
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## MEDICAL NEWS in brief

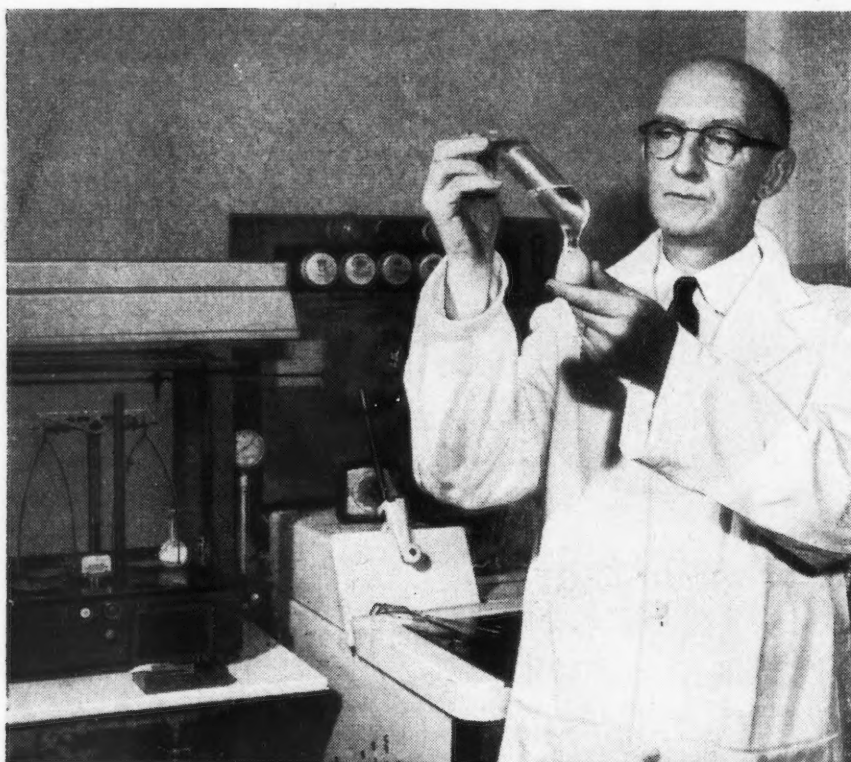
(Continued from page 50)

Institutions on the *Medical Horizons* roster include the Mayo Clinic, Johns Hopkins University, Kessler Institute, the Menninger Clinic, Meharry Medical College, the School of Medicine of the University of California at San Francisco, and Georgetown University.

### STEROIDS IN ULCERATIVE COLITIS

Brooke (*Lancet*, 2: 1175, 1956) points out a serious adverse effect

of cortisone and other steroids in some cases of ulcerative colitis. He has observed that where a patient with ulcerative colitis does not show definite improvement when corticosteroid therapy is prolonged for a month or longer, changes may occur in the colon wall such as to render surgery technically very difficult and highly hazardous. The wall becomes excessively friable and may actually disintegrate. Brooke suggests that steroid therapy should cease if no definite response is seen in cases of ulcerative colitis within one or two weeks.



W. D. LAVERTY—25 years milk laboratory experience—conducts quantitative butterfat test on evaporated milk using the Majonnier method and testing equipment.

## Just one of a number of checks

During processing, Farmer's Wife Formula Milks constantly undergo a number of tests in the plant and laboratory. Even after vacuum sealing in the most modern type of container, the quality of the individual can and contents is verified. It is this kind of constant check that leads doctors, paediatricians and hospitals from coast to coast to confidently recommend Farmer's Wife Formula Milks.

- Evaporated whole milk      • Concentrated skimmed milk
- Concentrated partly skimmed milk

# Farmer's Wife

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"Specialists in the Preparation of Milk Foods for Infant Feeding"

### TIN AND TAPEWORMS

From the University of Buenos Aires, Argentina (*Prensa méd. argent.*, 43: 2546, 1956), comes a report of studies of treatment of tapeworm infestation by a tin product containing the metal and the stannous oxide. A series of 58 patients were treated with different dosages. The most striking results were obtained with a high dose and in children. The success rate in adults was only 44%, but it was 100% in children treated with doses ranging from 2.5 g. per day at four years to about 8 g. per day at 15 years, which cleared out the tapeworm in every case. The great advantage of the treatment was the complete absence of side-effects, even in young children.

### ACADEMY OF MEDICINE OF CINCINNATI CENTENNIAL

The Academy of Medicine of Cincinnati, Ohio, cordially invites all physicians, their families, and their patients to its 100th Birthday Party, February 27-March 5, 1957. A Health Museum and Exposition will be established in Cincinnati's spacious and historic Music Hall, including 175 health and scientific exhibits and an atomic energy exhibit from the American Museum of Atomic Energy entitled "Atoms for Peace".

The Centennial Convocation will be held on the last night of the Exposition, March 5. The Convocation address will be given by Sir Edward Appleton, Nobel Laureate, Edinburgh, Scotland.

Professor Reginald McGrane, chairman of the Department of History, University of Cincinnati, has prepared a 100-year history of the Academy of Medicine, entitled "The Doctor's Forum". Copies of this volume will be available at the Centennial Exposition. The *Cincinnati Journal of Medicine* is also preparing a special Centennial Edition for the occasion.

### AWARDS FOR RESEARCH IN BASIC MEDICAL SCIENCES

The U.S. Public Health Service announces 44 five-year research fellowship awards to scientists in a number of universities and medical schools in the States and

also in Canada. The awards are the first in the new federal program designed to increase manpower for research in the basic medical sciences, and recipients are scientists who have completed a doctor's degree in biochemistry, pharmacology, physiology, microbiology, pathology or the psychological sciences. The fellowships are to permit recipients to continue research activities, together with appropriate teaching work. In this five-year plan the U.S. Public Health Service will award between 40 and 50 new fellowships every year until approximately 250 have been given. The Canadian recipients of fellowships are Dr. Alan B. Rothballer, Department of Anatomy, Albert Einstein College of Medicine; Harold J. Strecker, Department of Biochemistry in the same university; Jonathan B. Wittenberg, Department of Biochemistry in the same university.

#### FIRST PAN AMERICAN CANCER CYTOLOGY CONGRESS

An invitation is extended to all physicians interested in cancer diagnosis and research to attend the First Pan American Cancer Cytology Congress, to be held at Miami Beach, Florida, from April 25 to 29, 1957. Twenty-one nations of the western hemisphere have been invited to send representatives to the Congress.

The program will include the latest advances in cancer detection by cytological methods, radioisotopes, genetics, microbiology, the biology of cancer and research in leukaemia. Special emphasis will be placed upon gynaecological cancer and the revolutionary role of cervical cytology as a screening test for uterine cancer.

Of special interest to medical practitioners will be explanations of procedure and methods for the application of cytodagnosis for early detection of cancer in the physician's office.

Two awards of \$1,000 each—the Wien Awards for 1956 and 1957—will be presented at the conclusion of the Congress to the two scientists presenting papers whose work is judged to represent outstanding research in cancer cytology.


Physicians wishing to present scientific papers at the Congress should apply to the program chairman, Dr. Wayne Rogers, P.O. Box 633, Coral Gables, Florida. Inquiries about scientific exhibits or motion picture presentations should be addressed to the chairman, Dr. Homer L. Pearson, P.O. Box 633, Coral Gables, Florida.

#### A.M.A. COMMITTEE ON TOXICOLOGY

The Committee on Toxicology of the Council of Pharmacy and

Chemistry of the American Medical Association has discussed several important matters which are abstracted in brief in the November 3 issue of the *Journal of the American Medical Association*. A sub-committee on poisoning by kerosene was appointed to study measures for improving safety in the use of petroleum distillates. A monograph on kerosene poisoning is to be prepared, and methods for clinical evaluation of treatments and of laboratory investigation for quantitative analysis of kerosene were discussed. The Committee

(Continued on page 54)



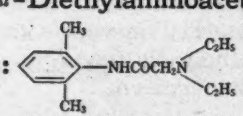
## XYLOCAINE® HCl SOLUTION

**Marks a New Era in Local Anesthesia**

**Xylocaine gives peak values in • Speed • Depth  
Duration • Clinical Effectiveness • Clinical Tolerance  
Stability • Versatility • Clinical Predictability • Safety**

<b>Trade Name:</b> XYLOCAINE	<b>Generic Name:</b> lidocaine*
<b>Chemical Name:</b> $\alpha$ -Diethylaminoaceto-2,6-xylylidide	

**Chemical Structure:**



**Potency:** Two to three times that of procaine.

**Duration of Action:** Two to three times that of procaine.

**Anesthetic Index:** 1.8.                      **Surface Anesthetic Index:** 8.

**Safety Factor:** Two to three times that of procaine (because smaller concentrations and volumes are clinically as effective).

**Sensitivity:** Allergic manifestations and sensitizing reactions have never been reported.


**Inhibition of Action of Sulfonamides or Antibiotics:** None.

**Versatility:** Effective in local infiltration anesthesia; in major conduction anesthesia; in temporary therapeutic blocks for relief of pain; in topical anesthesia.

**Supplied:** Vials, 0.5%, 1%, 2% in 20 cc., 50 cc. without and with epinephrine 1:100,000; also in cartridges, 1.8 cc. and ampoules, 2 cc., 2% without and with epinephrine 1:100,000.

**Astra Pharmaceuticals (Canada) Ltd., Toronto 4, Ont.**

\*CANADIAN PATENT NO. 503,645





## MEDICAL NEWS in brief

(Continued from page 53)

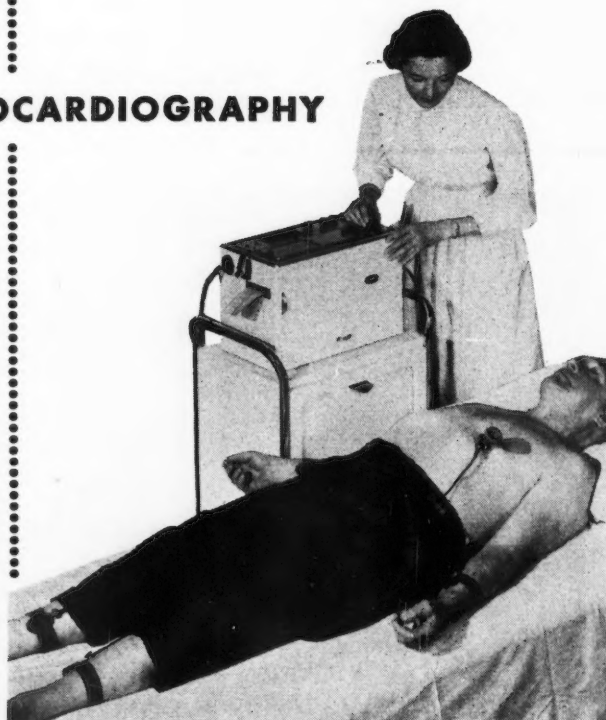
went on record as being strongly opposed to the use of vending machines for drugs in public places accessible to children, and against measures designed to tempt children to accept drugs as something

other than medication. There is no uniformity of legal or scientific opinion as to what constitutes a poison, and laws vary widely in their definition. The Committee felt that any substance which if improperly used could harm by chemical action should be provided

with an appropriate precautionary label. The Committee also considered public education about poisons and the operation of poison control centres; 13 out of the 17 operating centres in the U.S.A. sent in a report of their activities.

## OFFICE ELECTROCARDIOGRAPHY

*your  
patients  
are beginning  
to expect it.....*



Just as the "health I.Q." of the general public has increased in recent years, so also has the awareness of diagnostic and therapeutic measures been broadened. The authoritative reassurance of a cardiogram recorded in your own office can be as helpful to your patients as the early diagnosis of heart disease can be to your own clinical management.

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## ELECTROCARDIOGRAPH

— provides time-saving features and precision engineering for accurate, dependable diagnostic service. Timing and leads are marked automatically, and leads can be switched rapidly without base line shift or distortion. Preset controls simplify operation.

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Fisher & Burpe Limited, Winnipeg, Edmonton, Vancouver, Toronto  
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MEDICAL PUBLICATIONS  
IN CANADA

Little, Brown & Company of Boston and Toronto announce that their medical and scientific books will be distributed in the Dominion of Canada by the J. B. Lippincott Company of Montreal as of January 1, 1957. Little, Brown & Company feel that the distribution of their medical and scientific books in Canada by an organization exclusively devoted to the sale of this type of book will render better service to professors, students, physicians and scientists in Canada.

AMERICAN SOCIETY  
OF MAXILLOFACIAL  
SURGEONS

The American Society of Maxillofacial Surgeons will hold its next annual meeting at the Leamington Hotel, Minneapolis, Minnesota, May 12-15, 1957. The Secretary is Dr. John A. Drummond, 1414 Drummond Street, Montreal.

The Society also announces an Essay Contest for papers based on clinical and experimental research in maxillofacial surgery. Any medical graduate may submit a paper, which must be in triplicate and based on original work not previously published. The paper should be between 2,000 and 4,000 words in length. Closing date for submission of essays is April 15, 1957.

Certificates will be awarded to the authors of the two papers which the committee of judges consider best. The two winning papers are to be read by the authors before the Annual Meeting. Burroughs Wellcome & Co. (U.S.A.) Inc. has made \$300 available for the expenses of the winner, and \$200 will be awarded for expenses to the author of paper judged second. Further information may be obtained from the Secretary.

(Continued on page 56)

# Kolantyl + diet



## = sound ulcer therapy

provides prolonged relief of ulcer pain.<sup>1</sup>

*Kolantyl: 1. Neutralizes acid, 2. Inhibits pepsin, 3. Relieves hypermotility and spasm through musculotropic action, 4. Relieves spasm through neurotropic action, 5. Forms protecting demulcent, 6. Inhibits lysozyme.*

This combination of ulcer-combating ingredients in pleasant-tasting KOLANTYL Gel, or convenient tablets, makes rational its use as the medication of choice in peptic ulcer therapy.

### Rx Information Kolantyl

#### Gel and Tablets

##### Action:

*Bentylol\** content affords spasmolysis and parasympathetic-depressant actions without the side effects of atropine.

*Rapid, Prolonged Antacid Relief*  
... Balanced antacids — no laxation — no constipation

*Proven Demulcent Action...*  
Helps protect normal cells, encourages cellular repair

*Anti-enzyme Action...* Necrotic pepsin and lysozyme action checked

#### Composition:

Each 10 cc. of KOLANTYL Gel or each KOLANTYL tablet contains:  
Bentylol Hydrochloride...5 mg.  
Aluminum Hydroxide Gel .....400 mg.  
Magnesium Oxide .....200 mg.  
Sodium Lauryl Sulfate...25 mg.  
Methylcellulose .....100 mg.

#### Dosage:

Gel — 2 to 4 teaspoonfuls every three hours, or as needed. Tablets — 2 tablets (chewed for

more rapid action) every three hours, or as needed.

#### Supplied:

Gel — 12 oz. bottles.  
Tablets — bottles of 100 and 500.

1. Johnston, R. L.: J. Indiana St. M. A. 46:869, 1953. 2. McHardy, G., and Browne, D.: Southern M. J. 45:1139, 1952.

\*Merrell's distinctive antispasmodic that is more effective than atropine—free from side effects of atropine.<sup>2</sup>

THE WM. S. MERRELL COMPANY  
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New York, N. Y. • Cincinnati, Ohio



Pioneer in Medicine for Over 125 Years

TRADEMARKS: \*BENTYLOL\*, \*KOLANTYL\*



## MEDICAL NEWS in brief

(Continued from page 54)

ROYAL COLLEGE OF  
PHYSICIANS OF  
EDINBURGH

At a Quarterly Meeting of College held on Tuesday, November 6, 1956, the President, Sir Stanley Davidson, in the chair, the following were elected Fellows of the College: Gilbert Logie Adamson, M.D.(Man.), F.R.C.P.[C.]; Rus-

sell Johnson Collins, M.A., Western Reserve University, Cleveland, L.M.S. Nova Scotia, M.D. Western Reserve University, Cleveland, F.R.C.P.[C.], F.A.C.P.; and Russell Alfred Palmer, M.D., McGill, F.R.C.P.[C.], F.A.C.P.

ALCOHOL STUDIES  
AT YALE

Yale University announces its Summer School of Alcohol Studies

for July 1-27, 1957. This will be the 15th annual session of an interdisciplinary study of problems of alcohol and alcoholism in society. It will consist, as usual, of lectures and seminars under the direction of specialists, together with workshops for physicians, case workers, psychologists, clergy, educators and other leaders in society. Enrollment is limited to 200 students. Information may be obtained from the Registrar, Yale Summer School of Alcohol Studies, 52 Hillhouse Avenue, New Haven, Connecticut, U.S.A.

*Announcing the New*

# METAMINE<sup>®</sup> SUSTAINED

tablets of 10 mg.

triethanolamine trinitrate biphosphate

in the PROPHYLAXIS of  
ANGINA PECTORIS ATTACKS

1 tablet all day

1 tablet all night

Exerts prolonged action without deleterious effect.

Produces no significant change in the mean blood pressure level.

## Summary of a recent study on 103 patients:

"The 10 mg. sustained-release modification of triethanolamine trinitrate-biphosphate has demonstrated its clinical effectiveness in improving 80 (78 per cent) of 103 cases of angina pectoris, including a group refractory to other drugs of this type. This dosage form provided even more prolonged action than the usual long-acting nitrates, and consequently, a simplified dosage schedule was possible. No undesirable side reactions were observed in this series."

Fuller, H. L., and Kassel, L. E.: "Sustained-Release Triethanolamine Trinitrate Biphosphate (Metamine) in Angina Pectoris." *Antibiotic Medicine and Clinical Therapy*, Vol. 3, No. 5, Oct., 1956.

The Leeming Miles Co., Ltd., Montreal 28.

## XVIIe CONGRES D'OBSTETRIQUE ET DE GYNECOLOGIE DE LA FEDERATION DES SOCIETES DE LANGUE FRANCAISE

Le Congrès tiendra ses assises à la Faculté Mixte de Médecine et de Pharmacie Générales et Coloniales de Marseille du 9 au 12 septembre 1957.

Programme: Discussion des rapports (grossesse prolongée, synecies utérines, prolapsus après hystérectomie, insémination artificielle) et de communications relatives à ceux-ci; communications libres; expositions scientifiques et projections de films médicaux.

Ecrire au Secrétaire Général, M. le Professeur H. Serment, Hôpital de la Conception, Marseille, France.

## SYMPOSIUM ON COSMETICS

The Section on Pharmacy of the American Association for the Advancement of Science which met at the Hotel Statler, New York, on December 27, had in its program a symposium on cosmetics sponsored by the Committee on Cosmetics of the American Medical Association. This novel symposium included papers on the scientific formulation of cosmetics, the essentials of skin cleansing, the control of axillary sweating and body odours, the present status of pigment-forming drugs, and toxicity problems of cosmetics. The last paper was given by Dr. B. E. Conley of the American Medical Association.